

STIC Search Report Biotech-Chem Library

STIC Database Tracking Number

TO: Ralph J Gitomer Location: 3d65/3c18

Art Unit: 1655

Thursday, August 11, 2005

Case Serial Number: 10/648485

From: Noble Jarrell

Location: Biotech-Chem Library

Rem 1B71

Phone: 272-2556

Noble.jarrell@uspto.gov

Search Notes	
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10 . - P.

(FILE 'HOME' ENTERED AT 11:32:15 ON 11 AUG 2005)

FIRE THEAPLUS ENTERED AT 11:32:20 ON 11 AUG 2005 1 US2004038859/PN OR (JP2000-87574# OR WO2001-JP2507#)/AP,PRN

FILE 'REGISTRY' ENTERED AT 11:33:28 ON 11 AUG 2005

FILE 'HCAPLUS' ENTERED AT 11:33:31 ON 11 AUG 2005 TRA L1 1- RN : L_2

FILE REGISTRY ENTERED AT 11:33:31 ON 11 AUG 2005 3 SEAVIL 27

FILE !WPIX! ENTERED AT 11:33:34 ON 11 AUG 2005 _____1_L1__

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FILE COVERS 1907 - 11 Aug 2005 VOL 143 ISS 7 FILE LAST UPDATED: 10 Aug 2005 (20050810/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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- ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN L1
- 2001:717824 HCAPLUS AN
- 135:278068 DN
- ED Entered STN: 02 Oct 2001
- TI Skin basement membrane formation promoters containing matrix metalloprotease inhibitors and manufacture of artificial skin using the promoters
- IN Amano, Satoshi; Matsunaga, Yukiko; Inomata, Shinji
- PA Shiseido Co., Ltd., Japan
- Jpn. Kokai Tokkyo Koho, 17 pp. SO

CODEN: JKXXAF

- DT Patent
- LA Japanese
- IC
- ICM A61L027-00 ICS A61K045-00; A61K045-06; A61P017-00
- CC 63-7 (Pharmaceuticals)

Section cross-reference(s): 62

EAN CHT 1

PAIN	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	JP 2001269398	A2	20011002	JP 2000-87574	20000327 <

Search done by Noble Jarrell

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WO 2001-JP2507
                                                                  20010327 <--
     WO 2001072347
                         A1
                                20011004
         W: CN, KR, US
         RW: AT, BE, CH,
                        CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, TR
                                                                   20010327 <--
                         A1
                                20020220
                                            EP 2001-915860
     EP 1180371
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     US 2002193875
                         A1
                                20021219
                                            US 2001-979712
                                                                   20011126 <--
                                                                  20030827 <--
     US 2004038859
                                           US 2003-648485
                         A1
                                20040226
PRAI JP 2000-87574
                         Α
                                20000327
                                         <--
     WO 2001-JP2507
                         W
                                20010327
     US 2001-979712
                         A1
                                20011126
CLASS
 PATENT NO.
                CLASS PATENT FAMILY CLASSIFICATION CODES
                ____
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 JP 2001269398
                ICM
                       A61L027-00
                        A61K045-00; A61K045-06; A61P017-00
                ICS
                       A61K007/48; A61K007/48C22; A61K031/00+A; A61K038/55;
                ECLA
 WO 2001072347
                        A61K045/06; A61L027/54; A61L027/60
                ECLA
                        A61K031/00+A; A61K045/06; A61L027/22; A61L027/60
 EP 1180371
                        623/005.120; 424/439.000
 US 2002193875
                NCL
                 ECLA
                        A61K007/48; A61K007/48C22; A61K031/00+A; A61K038/55;
                        A61K045/06; A61L027/22; A61L027/54; A61L027/60
 US 2004038859
                NCL
                        514/001.000
                 ECLA
                        A61K007/48; A61K008/64; A61K031/00+A; A61K038/55;
                        A61K045/06; A61L027/22; A61L027/54; A61L027/60
     Skin basement membrane formation promoters and artificial skin formation
AB
     promoters contain matrix metalloprotease inhibitors and optionally matrix
     protein production promoters. Artificial skin is manufactured by adding matrix
     metalloprotease inhibitors and optionally matrix protein production promoters
     to a medium for artificial skin manufacture A skin model having stratified
     epidermis, obtained by culturing human foreskin-derived epidermal
     keratinocyte on contracted collagen gel, was further cultured in a medium
     containing CGS 27023A for 2 wk to form basement membrane structure. Plant
     exts., e.g those of Thymus serpyllum, Potentilla tormentilla, Thea
     sinensis, etc., had a similar effect. Cosmetic formulations containing the
     basement membrane formation promoters were also given.
     skin basement membrane formation promoter matrix metalloprotease
ST
     inhibitor; protein matrix prodn promoter skin basement membrane formation;
     artificial skin manuf matrix metalloprotease inhibitor
TT
     Skin
        (artificial; skin basement membrane formation promoters containing matrix
        metalloprotease inhibitors and optionally matrix protein production
        promoters for manufacture of artificial skin)
IT
     Proteins, specific or class
     RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL
     (Biological study); FORM (Formation, nonpreparative)
        (matrix, production promoters for; skin basement membrane formation
        promoters containing matrix metalloprotease inhibitors and optionally
        matrix protein production promoters for manufacture of artificial skin)
IT
     Basement membrane
        (skin basement membrane formation promoters containing matrix
        metalloprotease inhibitors and optionally matrix protein production
        promoters for manufacture of artificial skin)
IT
     Collagens, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (skin basement membrane formation promoters containing matrix
        metalloprotease inhibitors and optionally matrix protein production
        promoters for manufacture of artificial skin)
TT
     Lysophosphatidylcholines
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (soybean; skin basement membrane formation promoters containing matrix
        metalloprotease inhibitors for manufacture of artificial skin)
IT
     Transforming growth factors
```

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(α -; skin basement membrane formation promoters containing matrix metalloprotease inhibitors for manufacture of artificial skin) Transforming growth factors

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(β 1-; skin basement membrane formation promoters containing matrix metalloprotease inhibitors for manufacture of artificial skin) 141907-41-7

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; skin basement membrane formation promoters containing matrix metalloprotease inhibitors and optionally matrix protein production promoters for manufacture of artificial skin)

124168-73-6 169799-04-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(skin basement membrane formation promoters containing matrix metalloprotease inhibitors and optionally matrix protein production promoters for manufacture of artificial skin)

=> b reg

TT

тт

IT

FILE PREGISERY ENTERED AT 11:33:58 ON 11 AUG 2005
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STRUCTURE FILE UPDATES: 10 AUG 2005 HIGHEST RN 859511-21-0 DICTIONARY FILE UPDATES: 10 AUG 2005 HIGHEST RN 859511-21-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

505'EL 60E D C∈

L3 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN RN 169799-04-6 REGISTRY

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Entered STN: 08 Nov 1995
ED
     Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-
CN
     pyridinylmethyl)amino]-3-methyl-, monohydrochloride, (2R)- (9CI) (CA
     INDEX NAME)
OTHER NAMES:
     CGS 27023
CN
     CGS 27023A
CN
CN
    MMI 270
    MMI 270B
CN
FS
    STEREOSEARCH
DR
     161314-82-5, 204198-67-4
MF
     C18 H23 N3 O5 S . Cl H
SR
                 ADISINSIGHT, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS,
LC
       CASREACT, CIN, EMBASE, IMSRESEARCH, IPA, PROUSDDR, SYNTHLINE, TOXCENTER,
       USPAT2, USPATFULL
    (161314-70-1)
CRN
```

Absolute stereochemistry.

● HCl

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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**
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5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
              71 REFERENCES IN FILE CAPLUS (1907 TO DATE)
    ANSWER 2 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN
L3
     141907-41-7 REGISTRY
RN
     Entered STN: 19 Jun 1992
ED
     Proteinase, matrix metallo- (9CI) (CA INDEX NAME)
CN
OTHER NAMES:
    Matrix metalloendoproteinase
CN
CN
     Matrix metalloprotease
    Matrix metalloprotease HIPHUM35
CN
     Matrix metalloproteinase
CN
CN
     Matrix-degrading metalloproteinase
CN
     Matrixin
MF
     Unspecified
CI
     MAN
SR
     CA
                 ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS,
LC
       CEN, CIN, PROMT, TOXCENTER, USPAT2, USPATFULL
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71 REFERENCES IN FILE CA (1907 TO DATE)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3436 REFERENCES IN FILE CA (1907 TO DATE)
18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3447 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN

RN 124168-73-6 REGISTRY

ED Entered STN: 08 Dec 1989

CN D-Alaninamide, N-(4-aminobenzoyl)glycyl-L-prolyl-D-leucyl-N-hydroxy- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN FN 439

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C23 H34 N6 O6

CI COM

SR CA

LC STN Files: BIOSIS, CA, CAPLUS, CHEMCATS, TOXCENTER, USPATFULL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

Absolute stereochemistry.

- 13 REFERENCES IN FILE CA (1907 TO DATE)
- 13 REFERENCES IN FILE CAPLUS (1907 TO DATE)

अंद्रोहिल्ला ही रंद∈

ENGE OWNER ENTERED AT 11:34:02 ON 11 AUG 2005 COPYRIGHT (C) 2005 THE THOMSON CORPORATION

FILE LAST UPDATED: 10 AUG 2005 <20050810/UP>
MOST RECENT DERWENT UPDATE: 200551 <200551/DW>

DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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- >>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE http://thomsonderwent.com/coverage/latestupdates/ << <
- >>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
 GUIDES, PLEASE VISIT:
 http://thomsonderwent.com/support/userguides/ <<<
- >>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT
 DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX
 FIRST VIEW FILE WPIFV.
 FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv <<<

>>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501. PLEASE CHECK:

http://thomsonderwent.com/support/dwpiref/reftools/classification/code-revision/FOR DETAILS. <<<

'BIX BI, ABEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

90 6 611 14 tot

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ANSWER 1 OF 1 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
     2001-602815 [68]
                        WPIX
                        DNC C2001-178628
DNN N2001-449794
     Agents e.g. for promoting formation of skin basement membrane comprise
     matrix metalloprotease inhibitor.
DC
     B03 D21 P34
    AMANO, S; INOMATA, S; MATSUNAGA, Y
IN
     (SHIS) SHISEIDO CO LTD; (AMAN-I) AMANO S; (INOM-I) INOMATA S; (MATS-I)
PA
     MATSUNAGA Y
    24
CYC
                   A1 20011004 (200168)* JA
PΙ
     WO 2001072347
                                                35
                                                      A61L027-60
        RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
         W: CN KR US
                  A 20011002 (200172)
                                                17
                                                      A61L027-00
     JP 2001269398
                     A1 20020220 (200221) EN
                                                      A61L027-60
     EP 1180371
         R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR
     KR 2002019920 A 20020313 (200263)
                                                      A61L027-60
     CN 1365293
                    A 20020821 (200281)
                                                      A61L027-60
     US 2002193875
                    A1 20021219 (200303)
                                                      A61F002-14
     US 2004038859
                    A1 20040226 (200416)
                                                      A61K031-00
                                                                     <--
    WO 2001072347 A1 WO 2001-JP2507 20010327; JP 2001269398 A
     JP 2000-87574 20000327; EP 1180371 A1 EP 2001-915860 20010327,
     WO 2001-JP2507 20010327; KR 2002019920 A KR 2001-714980 20011123;
     CN 1365293 A CN 2001-800673 20010327; US 2002193875 A1 WO 2001-JP2507
     20010327, US 2001-979712 20011126; US 2004038859 A1 Cont of WO
     2001-JP2507 20010327, Cont of US 2001-979712 20011126, US 2003-648485
     20030827
     EP 1180371 A1 Based on WO 2001072347
FDT
PRAI JP 2000-87574
                         20000327
     ICM A61F002-14; A61K031-00; A61L027-00; A61L027-60
     ICS A61K007-00; A61K007-40; A61K007-48; A61K031-44; A61K035-78;
          A61K038-07; A61K045-00; A61K045-06; A61K047-00; A61L027-54;
          A61P017-00
     WO 200172347 A UPAB: 20050512
AB
     NOVELTY - Agents for promoting the formation of skin basement membrane or
     for promoting the formation of artificial skin comprise a matrix
     metalloprotease inhibitor.
          ACTIVITY - Dermatological.
          In an artificial skin production model using human dermal cells
     addition of CGS27023A (10 micro M) increased formation of artificial skin
     (no specific results given).
          MECHANISM OF ACTION - Matrix-Metalloproteinase-Inhibitor.
          USE - For promoting the formation of skin basement membrane or for
     promoting the formation of artificial skin.
     Dwq.0/4
     CPI GMPI
FS
FΑ
     AB; DCN
     CPI: B04-A10; B04-N04A; B14-D07C; B14-N17; B14-R01; D08-B09A
MC
=> b home
FILE 'HOME' ENTERED AT 11:34:08 ON 11 AUG 2005
=>
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=> b reg ENTER TRESISERY ENTERED AT 11:41:22 ON 11 AUG 2005 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2005 American Chemical Society (ACS)

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STRUCTURE FILE UPDATES: 10 AUG 2005 HIGHEST RN 859511-21-0 DICTIONARY FILE UPDATES: 10 AUG 2005 HIGHEST RN 859511-21-0

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TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

- % d 1de 117 for

- L7 ANSWER 1 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
- RN 208663-31-4 REGISTRY
- ED Entered STN: 19 Jul 1998
- CN Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](2-pyridinylmethyl)amino]-3-methyl-, (2S)- (9CI) (CA INDEX NAME)
- FS STEREOSEARCH
- MF C18 H23 N3 O5 S
- SR CA
- LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE) 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ANSWER 2 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN L7

RN

208663-30-3 REGISTRY Entered STN: 19 Jul 1998 ED

Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](2-CN pyridinylmethyl)amino]-3-methyl-, (2R)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C18 H23 N3 O5 S

CI COM

SR CA

CA, CAPLUS, CASREACT, PROUSDDR, SYNTHLINE, TOXCENTER LC STN Files:

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ANSWER 3 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN L7

RN 192570-31-3 REGISTRY

Entered STN: 14 Aug 1997 ED

Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-CN pyridinylmethyl)amino]-3-methyl-, (2S)- (9CI) (CA INDEX NAME) OTHER CA INDEX NAMES:

Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-CN

pyridinylmethyl) amino] -3-methyl-, (S)-

FS STEREOSEARCH

MF C18 H23 N3 O5 S

CI COM

SR

LC CA, CAPLUS, CASREACT, IMSRESEARCH, USPATFULL STN Files:

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 4 REFERENCES IN FILE CA (1907 TO DATE)
- 4 REFERENCES IN FILE CAPLUS (1907 TO DATE)
- L7 ANSWER 4 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
- RN 177701-98-3 REGISTRY
- ED Entered STN: 25 Jun 1996
- CN Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-
- pyridinylmethyl)amino]-3-methyl-, monohydrochloride (9CI) (CA INDEX NAME)
- DR 161441-84-5
- MF C18 H23 N3 O5 S . Cl H
- SR CA
- LC STN Files: CA, CAPLUS, IMSRESEARCH, TOXCENTER, USPATFULL
- CRN (709614-39-1)

HCl

- 5 REFERENCES IN FILE CA (1907 TO DATE)
- 5 REFERENCES IN FILE CAPLUS (1907 TO DATE)
- L7 ANSWER 5 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
- RN 177701-96-1 REGISTRY
- ED Entered STN: 25 Jun 1996
- CN Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-pyridinylmethyl)amino]-3-methyl-, (2R)-, (2Z)-2-butenedioate (salt) (9CI) (CA INDEX NAME)
- OTHER CA INDEX NAMES:
- CN Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3
 - pyridinylmethyl)amino]-3-methyl-, (R)-, (Z)-2-butenedioate (salt)
- FS STEREOSEARCH
- MF C18 H23 N3 O5 S . x C4 H4 O4
- SR CA
- LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

CM 1

CRN 161314-70-1 CMF C18 H23 N3 O5 S

Absolute stereochemistry.

CM 2

CRN 110-16-7 CMF C4 H4 O4

Double bond geometry as shown.

- 3 REFERENCES IN FILE CA (1907 TO DATE)
- 3 REFERENCES IN FILE CAPLUS (1907 TO DATE)
- L7 ANSWER 6 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
- RN
- 177701-95-0 REGISTRY Entered STN: 25 Jun 1996 ED
- Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-CN pyridinylmethyl)amino]-3-methyl-, (R)-, monomethanesulfonate (salt) (9CI) (CA INDEX NAME)
- FS STEREOSEARCH
- MF C18 H23 N3 O5 S . C H4 O3 S
- SR CA
- STN Files: CA, CAPLUS, TOXCENTER, USPATFULL LC

CM

CRN 161314-70-1 C18 H23 N3 O5 S CMF

Absolute stereochemistry.

CM

CRN 75-75-2 CMF C H4 O3 S

3 REFERENCES IN FILE CA (1907 TO DATE)

3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L7 ANSWER 7 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN

RN 177701-94-9 REGISTRY

ED Entered STN: 25 Jun 1996

CN Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-pyridinylmethyl)amino]-3-methyl-, (R)-, (2R,3R)-2,3-dihydroxybutanedioate (salt) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-pyridinylmethyl)amino]-3-methyl-, (R)-, [R-(R*,R*)]-2,3-dihydroxybutanedioate (salt)

FS STEREOSEARCH

MF C18 H23 N3 O5 S . x C4 H6 O6

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

CM 1

CRN 161314-70-1 CMF C18 H23 N3 O5 S

Absolute stereochemistry.

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

```
3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)
```

L7 ANSWER 8 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN 169799-04-6 REGISTRY RN ED Entered STN: 08 Nov 1995 CN Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3pyridinylmethyl)amino]-3-methyl-, monohydrochloride, (2R)- (9CI) (CA INDEX NAME) OTHER NAMES: CGS 27023 CN CGS 27023A CN CNMMI 270 MMI 270B CN FS STEREOSEARCH DR 161314-82-5, 204198-67-4 MF C18 H23 N3 O5 S . Cl H SR ADISINSIGHT, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, LC STN Files: CASREACT, CIN, EMBASE, IMSRESEARCH, IPA, PROUSDDR, SYNTHLINE, TOXCENTER,

Absolute stereochemistry.

(161314-70-1)

CRN

USPAT2, USPATFULL

● HCl

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

71 REFERENCES IN FILE CA (1907 TO DATE) 5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA 71 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ANSWER 9 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN L7 161314-70-1 REGISTRY RN ED Entered STN: 08 Mar 1995 CNButanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3pyridinylmethyl)amino]-3-methyl-, (2R)- (9CI) (CA INDEX NAME) OTHER CA INDEX NAMES: Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-CN pyridinylmethyl)amino]-3-methyl-, (R)-

FS STEREOSEARCH

MF C18 H23 N3 O5 S

CI COM

SR CA

CA, CAPLUS, CASREACT, IMSDRUGNEWS, IMSRESEARCH, PROUSDDR, LC STN Files:

TOXCENTER, USPATFULL

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 17 REFERENCES IN FILE CA (1907 TO DATE)
- 17 REFERENCES IN FILE CAPLUS (1907 TO DATE)
- L7 ANSWER 10 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
- RN 161313-61-7 REGISTRY
- ED Entered STN: 08 Mar 1995
- CN Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](2-pyridinylmethyl)amino]-3-methyl-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)
- FS STEREOSEARCH
- MF C18 H23 N3 O5 S . C1 H
- SR CA
- LC STN Files: CA, CAPLUS, PROUSDDR, SYNTHLINE, TOXCENTER, USPATFULL
- CRN (208663-30-3)

Absolute stereochemistry.

HCl

- 4 REFERENCES IN FILE CA (1907 TO DATE)
- 4 REFERENCES IN FILE CAPLUS (1907 TO DATE)
- L7 ANSWER 11 OF 11 REGISTRY COPYRIGHT 2005 ACS on STN
- RN 161313-56-0 REGISTRY
- ED Entered STN: 08 Mar 1995
- CN Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-pyridinylmethyl)amino]-3-methyl-, monohydrochloride, (S)- (9CI) (CA INDEX NAME)
- FS STEREOSEARCH

MF C18 H23 N3 O5 S . Cl H

SR CA

LC STN Files: CA, CAPLUS, IMSRESEARCH, TOXCENTER, USPATFULL

CRN (192570-31-3)

Absolute stereochemistry.

HC1

- 4 REFERENCES IN FILE CA (1907 TO DATE)
- 4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

de hystation

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L6

L7

L8

L9

(FILE 'HOME' ENTERED AT 11:32:15 ON 11 AUG 2005)

FILE 'HCAPLUS' ENTERED AT 11:32:20 ON 11 AUG 2005 1 SEA ABB=ON PLU=ON US2004038859/PN OR (JP2000-87574# OR L1 WO2001-JP2507#)/AP,PRN

FILE 'REGISTRY' ENTERED AT 11:33:28 ON 11 AUG 2005

FILE 'HCAPLUS' ENTERED AT 11:33:31 ON 11 AUG 2005 L2 TRA L1 1- RN : 3 TERMS

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FILE 'WPIX' ENTERED AT 11:33:34 ON 11 AUG 2005 1 SEA ABB=ON PLU=ON US2004038859/PN OR (JP2000-87574# OR WO2001-JP2507#)/AP, PRN

FIME REGISTRY' ENTERED AT 11:36:03 ON 11 AUG 2005 **L**5

1 SEA ABB=ON PLU=ON C18H23N3O5S AND L3 34 SEA ABB=ON PLU=ON C18H23N3O5S AND NC5/ES AND 46.150.18/RID D STR TOT

SEL RN 19 20 22-26 28 30-32 L6

11 SEA ABB=ON PLU=ON (161313-56-0/BI OR 161313-61-7/BI OR 161314-70-1/BI OR 169799-04-6/BI OR 177701-94-9/BI OR 177701-95 -0/BI OR 177701-96-1/BI OR 177701-98-3/BI OR 192570-31-3/BI OR 208663-30-3/BI OR 208663-31-4/BI) AND L6

FILE 'HCAPLUS' ENTERED AT 11:42:11 ON 11 AUG 2005

85 SEA ABB=ON PLU=ON L7

90 SEA ABB=ON PLU=ON MMI270# OR MMI(1A) (270# OR 270 (1A)B) OR CGS27023# OR CGS27(1A)023# OR CGS(1A)(27023# OR 27(1A)023#)

L10 115 SEA ABB=ON PLU=ON (L8 OR L9)

E AMANO S/AU

65 SEA ABB=ON PLU=ON "AMANO S"/AU L11

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L12
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L15
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                E SHISEIDO/CS, PA
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L24
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L25
                E BASEMENT MEMBRANE/CT
                E E3+ALL
           5462 SEA ABB=ON PLU=ON BASEMENT MEMBRANE+OLD/CT
L26
                E COLLAGEN/CT
                E E3+ALL
                E E2+ALL
          87537 SEA ABB=ON PLU=ON COLLAGENS+OLD, NT/CT
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0 SEA ABB=ON PLU=ON L29 AND SKIN
L31
L32
=> b hcap
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FILE COVERS 1907 - 11 Aug 2005 VOL 143 ISS 7 FILE LAST UPDATED: 10 Aug 2005 (20050810/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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L20 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2003:96165 HCAPLUS
DN
     138:142206
ED
     Entered STN: 07 Feb 2003
TI
     Skin vitalizing composition for external use anti-aging preparation
     Amano, Satoshi; Ogura, Yuki; Matsunaga, Yukiko; Tsuda,
IN
     Takanari; Aoyama, Yukari; Koga, Nobuyoshi
PΑ
     Shiseido Company Limited, Japan
SO
     Eur. Pat. Appl., 30 pp.
     CODEN: EPXXDW
DТ
    Patent
    English
LΑ
IC
     ICM A61K007-48
     62-4 (Essential Oils and Cosmetics)
CC
     Section cross-reference(s): 63
FAN.CNT 1
                                                                 DATE
                                           APPLICATION NO.
     PATENT NO.
                        KIND DATE
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                               20030205
                                           EP 2002-292849
                                                                  20021115
    EP 1281396
                         A2
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            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     JP 2004075661
                               20040311
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                                                                  20021106
                        A2
     US 2004001897
                        A1
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     CN 1465338
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PRAI JP 2002-177601
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                               20021209
CLASS
                CLASS PATENT FAMILY CLASSIFICATION CODES
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                       A61K007-48
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                       A61K008/55C; A61K008/64; A61K008/97; A61K008/98C6;
 EP 1281396
                ECLA
                       A61Q019/00; A61Q019/08
 JP 2004075661 FTERM 4C081/AB19; 4C081/CD121; 4C081/EA05; 4C084/AA02;
                       4C084/AA03; 4C084/AA17; 4C084/AA20; 4C084/BA01;
                       4C084/BA08; 4C084/BA20; 4C084/DA13; 4C084/DB52;
                       4C084/DB55; 4C084/MA02; 4C084/MA63; 4C084/NA14;
                        4C084/ZA891; 4C084/ZB221; 4C084/ZC201; 4C084/ZC751;
                        4C086/AA01; 4C086/AA02; 4C086/DA41; 4C086/MA03;
                       4C086/MA04; 4C086/MA63; 4C086/NA14; 4C086/ZA89; 4C086/ZB22; 4C086/ZC75; 4C088/AB12; 4C088/AB38;
                        4C088/CA03; 4C088/MA08; 4C088/MA63; 4C088/NA14;
                        4C088/ZA89; 4C088/ZB22; 4C088/ZC75
 US 2004001897
                 NCL
                        424/745.000; 435/212.000
                       A61K008/55C; A61K008/64; A61K008/97; A61K008/98C6;
                ECLA
                       A61Q019/00; A61Q019/08
 US 2005089516
                NCL
                        424/094.640
                       A61K008/55C; A61K008/64; A61K008/97; A61K008/98C6;
                ECLA
                       A61Q019/00; A61Q019/08
AB
     The invention provides an epidermal basement membrane structure formation
     protease inhibitor, and optionally an accelerator of production of
     extracellular matrix protein components of the epidermal basement
```

The invention provides an epidermal basement membrane structure formation accelerating preparation and a skin external preparation comprising a serine protease inhibitor, and optionally an accelerator of production of extracellular matrix protein components of the epidermal basement membrane. It also provides, as a means for producing artificial skin having an adequately formed basement membrane, an artificial skin-forming medium which comprises a serine protease inhibitor, and optionally an accelerator of production of extracellular matrix protein components of the epidermal basement membrane and a matrix metalloprotease inhibitor, as well as a method for producing the same.

```
proteinase inhibitor lysophospholipid antiaging cosmetic; basement
ST
     membrane skin epidermis antiaging cosmetic; extracellular matrix protein
    antiaging cosmetic; skin transplant proteinase inhibitor
TΤ
    Laminins
     RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
        (5; skin vitalizing composition for external use antiaging preparation containing
        proteinase inhibitors and lysophospholipids)
IT
    Cosmetics
        (antiaging; skin vitalizing composition for external use antiaging preparation
        containing proteinase inhibitors and lysophospholipids)
IT
    Skin
        (artificial, culturing of; skin vitalizing composition for external use
        antiaging preparation and artificial skin containing proteinase inhibitors)
IT
    Cosmetics
        (creams; skin vitalizing composition for external use antiaging preparation
        containing proteinase inhibitors and lysophospholipids)
IT
    Cosmetics
        (emulsions; skin vitalizing composition for external use antiaging preparation
        containing proteinase inhibitors and lysophospholipids)
TT
     Skin
        (epidermis, basement membranes, accelerators of production of; skin
        vitalizing composition for external use antiaging preparation containing proteinase
        inhibitors and lysophospholipids)
ΙT
     Proteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (extracellular matrix-associated, accelerators of production of; skin
        vitalizing composition for external use antiaging preparation containing proteinase
        inhibitors and lysophospholipids)
IT
    Mentha
        (exts.; skin vitalizing composition for external use antiaging preparation
containing
        proteinase inhibitors and lysophospholipids)
IT
        (foundations; skin vitalizing composition for external use antiaging preparation
        containing proteinase inhibitors and lysophospholipids)
IT
     Fagus
        (lysophospholipids of; skin vitalizing composition for external use
        antiaging preparation containing proteinase inhibitors and lysophospholipids)
IT
     Basement membrane
        (skin epidermis, accelerators of production of; skin vitalizing composition for
        external use antiaging preparation containing proteinase inhibitors and
        lysophospholipids)
IT
     Interleukin 1
     Lysophospholipids
     Platelet-derived growth factors
     RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
        (skin vitalizing composition for external use antiaging preparation containing
        proteinase inhibitors and lysophospholipids)
IT
     Transplant and Transplantation
        (skin; skin vitalizing composition for external use antiaging preparation and
        artificial skin containing proteinase inhibitors)
     Lysophosphatidylcholines
IT
     RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
        (soybean; skin vitalizing composition for external use antiaging preparation
        containing proteinase inhibitors and lysophospholipids)
IT
     Skin
        (transplant; skin vitalizing composition for external use antiaging preparation
        and artificial skin containing proteinase inhibitors)
IT
     Collagens, biological studies
     RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
        (type IV; skin vitalizing composition for external use antiaging preparation
        containing proteinase inhibitors and lysophospholipids)
TT
     Collagens, biological studies
     RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
        (type VII; skin vitalizing composition for external use antiaging preparation
        containing proteinase inhibitors and lysophospholipids)
```

IT Transforming growth factors RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses) $(\alpha$ -; skin vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids) 37259-58-8, Serine protease 141907-41-7, Matrix metalloprotease IT RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; skin vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids) 9087-70-1, Aprotinin 177701-98-3 IT RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (skin vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids) TT 177701-98-3 RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (skin vitalizing composition for external use antiaging preparation containing proteinase inhibitors and lysophospholipids) RN 177701-98-3 HCAPLUS Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-CN pyridinylmethyl)amino]-3-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

HCl

ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN L20 2003:79438 HCAPLUS ΑN 138:398112 DN Entered STN: 02 Feb 2003 Possible involvement of gelatinases in basement membrane damage and ΤI wrinkle formation in chronically ultraviolet B-exposed hairless mouse ΑU Inomata, Shinji; Matsunaga, Yukiko; Amano, Satoshi; Takada, Keiko; Kobayashi, Kouji; Tsunenaga, Makoto; Nishiyama, Toshio; Kohno, Yoshiyuki; Fukuda, Minoru Skincare Ingredient Research Laboratories, Shiseido Life Science CS Research Center, Yokohama, 224-8558, Japan SO Journal of Investigative Dermatology (2003), 120(1), 128-134 CODEN: JIDEAE; ISSN: 0022-202X Blackwell Publishing, Inc. PB DTJournal LΑ English CC 8-6 (Radiation Biochemistry) A number of studies indicate that matrix metalloproteinase might be involved AΒ in photoaging, but little is known about their direct contribution to UV-induced histol. and morphol. changes in the skin in vivo. This study reports the relationship between changes of matrix metalloproteinase activities and UV B-induced skin changes in hairless mouse. The role of matrix metalloproteinase in the skin changes was studied by topical application of a specific matrix metalloproteinase inhibitor. The backs of mice were exposed to UV B three times a week for 10 wk. Histol. studies showed that the basement membrane structure was damaged, with

epidermal hyperplasia, in the first 2 wk of UV B irradiation, followed by the appearance of wrinkles, which gradually extended in the latter half of the UV B irradiation period. We observed enhancement of type IV collagen degradation activity, but not collagenase or matrix metalloproteinase-3 activity, in exts. of UV B-irradiated, wrinkle-bearing skin. Gelatin zymog. anal. revealed that gelatinases, matrix metalloproteinase-9 and matrix metalloproteinase-2, were significantly increased in the extract zymog. study clarified that the activity was specifically localized in whole epidermis of UV B-irradiated, wrinkled skin in comparison with normal skin. The activity was induced around the basal layer of the epidermis by a single UV exposure of at least one minimal erythema dose. Furthermore, topical application of a specific matrix metalloproteinase inhibitor, CGS27023A, inhibited UV B-induced gelatinase activity in the epidermis, and its repeated application prevented UV B-induced damage to the basement membrane, as well as epidermal hyperplasia and dermal collagen degradation UV B-induced wrinkles were also prevented by administration of the inhibitor. These results, taken together, suggest that UV B-induced enhancement of gelatinase activity in the skin contributes to wrinkle formation through the destruction of basement membrane structure and dermal collagen in chronically UV B-exposed hairless mouse, and thus topical application of matrix metalloproteinase inhibitors may be an effective way to prevent UV B-induced wrinkle formation.

gelatinase basement membrane skin wrinkle formation chronic UVB exposure; ST photoprotectant matrix metalloproteinase inhibitor

IT Hyperplasia

> (epidermal; gelatinases involvement in basement membrane damage and wrinkle formation in chronic UVB exposure)

TT Skin, disease

(epidermis, hyperplasia; gelatinases involvement in basement membrane damage and wrinkle formation in chronic UVB exposure)

Basement membrane тт

UV B radiation

(gelatinases involvement in basement membrane damage and wrinkle formation in chronic UVB exposure)

IT Skin, disease

(photoaging, wrinkles; gelatinases involvement in basement membrane damage and wrinkle formation in chronic UVB exposure)

TT Collagens, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study) (type IV; gelatinases involvement in basement membrane damage and wrinkle formation in chronic UVB exposure)

9001-12-1, Collagenase 79955-99-0, Matrix metalloproteinase-3 TT 146480-35-5, Matrix metalloproteinase-2 146480-36-6, Matrix metalloproteinase-9

RL: BSU (Biological study, unclassified); BIOL (Biological study) (gelatinases involvement in basement membrane damage and wrinkle formation in chronic UVB exposure)

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L20 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
     2002:675789 HCAPLUS
AN
     137:221767
DN
ED
     Entered STN: 08 Sep 2002
     Method for suppressing reduction of elasticity of skin
TI
     Ochiai, Nobuhiko; Inomata, Shinji; Takada, Keiko
IN
PA
     Shiseido Company, Ltd., Japan
     PCT Int. Appl., 28 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LА
     Japanese
     ICM A61K007-00
IC
     ICS A61K007-48; A61K007-40; A61K035-78; A61K045-00; A61P005-30;
          A61P017-00
CC
     62-4 (Essential Oils and Cosmetics)
FAN.CNT 1
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                                             APPLICATION NO.
                                                                      DATE
     PATENT NO.
                                 DATE
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     JP 2002255850
                           A2
                                  20020911
                                             EP 2002-700812
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     EP 1396255
                           A1
                                  20040310
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                                                                       20030826
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PRAI JP 2001-50839
                           Α
                                  20010226
     WO 2002-JP1757
                                  20020226
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                         A61K007-00
                         A61K007-48; A61K007-40; A61K035-78; A61K045-00;
                  ICS
                         A61P005-30; A61P017-00
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A61K008/49C4; A61K008/97; A61Q019/00
 WO 2002067873
                 ECLA
                        A61K008/49C4; A61K008/97; A61Q019/00; A61Q019/08
                 ECLA
 EP 1396255
US 2004077523
                 NCL
                        514/001.000
                        A61K008/49C4; A61K008/97; A61Q019/00; A61Q019/08
                 ECLA.
    The invention relates to a method for prevention of skin elasticity
AB
     decrease due to lack of female sex hormones in relation to ovarian
     function disorder, e.g. menopause, wherein the method includes treatment
     of the skin with matrix metalloproteinase inhibitor. A cream containing
    N-hydroxy-2(R) [(4-methoxyphenyl)sulfonyl](3-picolyl)-methylbutanamide
    hydrochloride 1, stearic acid 5, stearyl alc. 4, isopropylmyristate 18,
     glycerin monostearate 3, propylene glycol 10, KOH 0.2, sodium
     hydrogensulfite 0.01, preservative and fragrance q.s., and water balance
     to 100 % was prepared
     matrix metalloproteinase inhibitor skin elasticity improvement
ST
IT
     Cosmetics
        (antiaging; prevention of skin elasticity decrease with matrix
        metalloproteinase inhibitors)
IT
     Cosmetics
        (creams; prevention of skin elasticity decrease with matrix
        metalloproteinase inhibitors)
IT
     Cosmetics
        (emulsions; prevention of skin elasticity decrease with matrix
        metalloproteinase inhibitors)
IT
     Garcinia mangostana
        (exts.; prevention of skin elasticity decrease with matrix
        metalloproteinase inhibitors)
TΤ
     Ovary, disease
        (failure; prevention of skin elasticity decrease due to lack of female
        sex hormones with matrix metalloproteinase inhibitors)
TT
     Cosmetics
        (foundations; prevention of skin elasticity decrease with matrix
        metalloproteinase inhibitors)
IT
        (gels; prevention of skin elasticity decrease with matrix
        metalloproteinase inhibitors)
IT
     Cosmetics
        (lotions; prevention of skin elasticity decrease with matrix
        metalloproteinase inhibitors)
IT
        (packs; prevention of skin elasticity decrease with matrix
        metalloproteinase inhibitors)
IT
        (prevention of skin elasticity decrease due to lack of female sex
        hormones with matrix metalloproteinase inhibitors)
IT
     Estrogens
     Progestogens
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (prevention of skin elasticity decrease due to lack of female sex
        hormones with matrix metalloproteinase inhibitors)
                             141907-41-7, Matrix metalloproteinase
ΙT
     9040-48-6, Gelatinase
     146480-36-6, MMP-9
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (prevention of skin elasticity decrease with matrix metalloproteinase
        inhibitors)
TT
     169799-04-6
     RL: COS (Cosmetic use); PAC (Pharmacological activity); BIOL (Biological
     study); USES (Uses)
        (prevention of skin elasticity decrease with matrix metalloproteinase
        inhibitors)
IT
     169799-04-6
     RL: COS (Cosmetic use); PAC (Pharmacological activity); BIOL (Biological
     study); USES (Uses)
        (prevention of skin elasticity decrease with matrix metalloproteinase
        inhibitors)
     169799-04-6 HCAPLUS
RN
     Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-
```

pyridinylmethyl)amino]-3-methyl-, monohydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

HCl

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L20 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2001:873192 HCAPLUS
DN
     136:10927
     Entered STN: 04 Dec 2001
ED
ΤI
     Cosmetics containing sulfonylhydroxamic acids
     Inomata, Shinji; Kobayashi, Koji; Amano, Satoshi;
IN
     Fukunishi, Hirotada
     Shiseido Co., Ltd., Japan
PΑ
so
     Jpn. Kokai Tokkyo Koho, 9 pp.
     CODEN: JKXXAF
DΤ
     Patent
LΑ
     Japanese
     ICM A61K031-18
IC
     ICS A61K007-00; A61K031-19; A61K031-4406; A61P017-00; A61P043-00;
          C07D213-42
CC
     62-4 (Essential Oils and Cosmetics)
FAN CNT 1
                                           APPLICATION NO.
                                                                  DATE
     PATENT NO.
                        KIND
                                DATE
                                20011204
                                                                  20000526
     JP 2001335478
                         A2
                                            JP 2000-197310
                                20000526
PRAI JP 2000-197310
CLASS
                CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
                       ______
                _ - - - -
 JP 2001335478
                ICM
                       A61K031-18
                        A61K007-00; A61K031-19; A61K031-4406; A61P017-00;
                 ICS
                       A61P043-00; C07D213-42
OS
     MARPAT 136:10927
     This invention relates to antiaging and skin-moisturizing cosmetics
AB
     comprising sulfonylhydroxamic acids as matrix metalloprotease inhibitors.
     Preferred compds. include (2R)-N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-
     pyridinylmethyl)amino]-3-methylbutanamide and N-[4-[[[2-(hydroxyamino)-2-
     oxoethyl]amino]sulfonyl]phenyl]-4-methylbenzamide.
ST
     antiaging moisturizing cosmetic sulfonylhydroxamic acid
IT
     Cosmetics
        (antiaging; antiaging cosmetics containing sulfonylhydroxamic acids as
        matrix metalloprotease inhibitors)
IT
     Cosmetics
        (moisturizers; antiaging cosmetics containing sulfonylhydroxamic acids as
        matrix metalloprotease inhibitors)
     161314-70-1 169799-04-6 188131-48-8
                                             375859-53-3
IT
     RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
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(antiaging cosmetics containing sulfonylhydroxamic acids as matrix metalloprotease inhibitors)

IT 141907-41-7, Matrix metalloprotease

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; antiaging cosmetics containing sulfonylhydroxamic acids as matrix metalloprotease inhibitors)

IT 161314-70-1

RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
(antiaging cosmetics containing sulfonylhydroxamic acids as matrix
metalloprotease inhibitors)

RN 161314-70-1 HCAPLUS

CN Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3pyridinylmethyl)amino]-3-methyl-, (2R)- (9CI) (CA INDEX NAME)

L20 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

Absolute stereochemistry.

```
AN
    2001:868173 HCAPLUS
DN
    136:10912
    Entered STN: 30 Nov 2001
ED
    Skin compositions containing matrix metalloproteinase inhibitor for
ΤI
    suppressing sebum secretion
IN
    Inomata, Shinji; Kobayashi, Koji
    Shiseido Company, Ltd., Japan
PA
    PCT Int. Appl., 26 pp.
SO
    CODEN: PIXXD2
DT
    Patent
LA
    Japanese
IC
    ICM A61K007-48
    ICS A61K031-12; A61K031-4406; A61K035-78; A61K045-00; A61P017-00
CC
    62-4 (Essential Oils and Cosmetics)
FAN.CNT 1
                                         APPLICATION NO.
                                                                DATE
    PATENT NO.
                       KIND
                              DATE
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    WO 2001089471
                        A2
                              20011129
                                          WO 2001-JP4336
                                                                20010523
PΙ
    WO 2001089471
                              20020718
                        A3
        W: CN, KR, US
        RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR
    JP 2002047125
                                          JP 2001-151391
                                                                20010521
                        A2
                              20020212
    EP 1284134
                        A2
                              20030219
                                          EP 2001-932233
                                                                20010523
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, FI, CY, TR
                                          US 2002-277000
                                                                20021120
    US 2004009241
                        A1
                              20040115
PRAI JP 2000-197309
                        Α
                              20000526
    JP 2001-151391
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                              20010521
                              20010523
                        W
    WO 2001-JP4336
CLASS
                CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
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 WO 2001089471 ICM
                      A61K007-48
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ICS
                        A61K031-12; A61K031-4406; A61K035-78; A61K045-00;
                        A61P017-00
WO 2001089471
                 ECLA
                        A61K007/48W4; A61K008/49C6; A61K008/97; A61K031/12;
                        A61K031/4406; A61Q001/02; A61Q019/00; A61Q019/08
                        A61K008/02F; A61K008/49C6; A61K008/97; A61K031/12;
EP 1284134
                 ECLA
                        A61K031/4406; A61Q001/02; A61Q019/00; A61Q019/08
US 2004009241
                 NCL
                        424/725.000; 514/575.000; 424/739.000
                        A61K008/02F; A61K008/49C6; A61K008/97; A61K031/12;
                 ECLA
                        A61K031/4406; A61Q001/02; A61Q019/00; A61Q019/08
AΒ
    Disclosed are external skin compns. for suppressing sebum secretion which
     contain a metalloproteinase inhibitor. The effect of a compound
     N-hydroxy-2(R)-[[(4-methoxyphenyl)sulfonyl]3-picolyl]-3-methylbutanamide
     hydrochloride (I) on sebum secretion in hairless mouse was examined Also, a
     skin cream containing I 1 % was formulated.
     metalloproteinase inhibitor cosmetic sebum suppression; gelatinase
     inhibitor cosmetic sebum suppression
IT
     Cosmetics
        (creams; skin compns. containing matrix metalloproteinase inhibitor for
        suppressing sebum secretion)
IT
     Cosmetics
        (emulsions; skin compns. containing matrix metalloproteinase inhibitor for
        suppressing sebum secretion)
ΙT
    Blumea balsamifera
     Cinnamomum cassia
     Cocos nucifera
    Garcinia mangostana
     Persea americana
     Potentilla tormentilla
        (exts.; skin compns. containing matrix metalloproteinase inhibitor for
        suppressing sebum secretion)
TT
     Cosmetics
        (foundations; skin compns. containing matrix metalloproteinase inhibitor
        for suppressing sebum secretion)
тт
     Cosmetics
        (gels; skin compns. containing matrix metalloproteinase inhibitor for
        suppressing sebum secretion)
IT
     Cosmetics
        (packs; skin compns. containing matrix metalloproteinase inhibitor for
        suppressing sebum secretion)
TΤ
     Sebum
        (skin compns. containing matrix metalloproteinase inhibitor for suppressing
        sebum secretion)
                             141907-41-7, Matrix Metalloproteinase
IT
     9040-48-6, Gelatinase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (skin compns. containing matrix metalloproteinase inhibitor for suppressing
        sebum secretion)
\mathbf{IT}
     458-37-7, Curcumin 161314-70-1
     RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
        (skin compns. containing matrix metalloproteinase inhibitor for suppressing
        sebum secretion)
TT
     161314-70-1
     RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)
        (skin compns. containing matrix metalloproteinase inhibitor for suppressing
        sebum secretion)
RN
     161314-70-1 HCAPLUS
     Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-
CN
     pyridinylmethyl)amino]-3-methyl-, (2R)- (9CI) (CA INDEX NAME)
```

Absolute stereochemistry.

L20 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:855224 HCAPLUS

DN 136:197396

ED Entered STN: 27 Nov 2001

TI Importance of Balance between Extracellular Matrix Synthesis and Degradation in Basement Membrane Formation

AU Amano, Satoshi; Akutsu, Nobuko; Matsunaga, Yukiko; Kadoya, Kuniko; Nishiyama, Toshio; Champliaud, Marie-France; Burgeson, Robert E.; Adachi, Eijiro

CS Shiseido Life Science Research Center, Yokohama, 236-8643, Japan

SO Experimental Cell Research (2001), 271(2), 249-262 CODEN: ECREAL; ISSN: 0014-4827

PB Academic Press

DT Journal

LA English

CC 13-2 (Mammalian Biochemistry)

The epidermal basement membrane (BM) plays important roles in adhesion AB between epidermis and dermis and in controlling epidermal differentiation. In a skin-equivalent (SE), components of the epidermal BM such as laminin 5 and type IV and VII collagens were detected in conditioned media and in basal keratinocytes. Despite production of these BM components, however, BM was rarely observed at the dermal-epidermal junction. One possible explanation for the absence of BM in SEs is that matrix metalloproteinases (MMPs) degrade newly synthesized extracellular matrixes. In fact, several MMPs, such as MMPs-1, 2, 3, and 9, were observed to be present in conditioned media and some of them were in active forms. Tissue inhibitor of metalloproteinase (TIMP)-2 was not detected, although TIMP-1 was present. BM degradation activity presumably exceeds BM formation activity in the SE, resulting in the absence of lamina densa at the dermal-epidermal junction. Synthetic MMP inhibitors ${\tt CGS27023A}$ and MMP inhibitor I, which inhibit MMPs 1, 2, 3, and 9, markedly augmented deposition of laminin 5 and type IV and VII collagens at the dermal-epidermal junction, resulting in formation of continuous epidermal BM. These results suggest that the balance between synthesis and degradation of BM components is important for BM formation. (c) 2001 Academic Press.

ST laminin collagen metalloproteinase extracellular matrix formation basement membrane epidermis

IT Laminins

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(5; balance between synthesis of extracellular matrix components and their degradation by matrix metalloproteinases in basement membrane formation at dermal-epidermal junction)

IT Basement membrane

Extracellular matrix

(balance between synthesis of extracellular matrix components and their degradation by matrix metalloproteinases in basement membrane formation at dermal-epidermal junction)

IT Skin

(dermis; balance between synthesis of extracellular matrix components and their degradation by matrix metalloproteinases in basement membrane

Gitomer 10 / 648485 formation at dermal-epidermal junction) IT Skin (epidermis; balance between synthesis of extracellular matrix components and their degradation by matrix metalloproteinases in basement membrane formation at dermal-epidermal junction) TT Skin (keratinocyte; balance between synthesis of extracellular matrix components and their degradation by matrix metalloproteinases in basement membrane formation at dermal-epidermal junction) ΙT Collagens, biological studies RL: BSU (Biological study, unclassified); BIOL (Biological study) (type IV; balance between synthesis of extracellular matrix components and their degradation by matrix metalloproteinases in basement membrane formation at dermal-epidermal junction) Collagens, biological studies IT RL: BSU (Biological study, unclassified); BIOL (Biological study) (type VII; balance between synthesis of extracellular matrix components and their degradation by matrix metalloproteinases in basement membrane formation at dermal-epidermal junction) TT 9001-12-1, Matrix metalloproteinase-1 79955-99-0, Matrix 140208-24-8, TIMP-1 146480-35-5, Matrix metalloproteinase-3 metalloproteinase-2 146480-36-6, Matrix metalloproteinase-9 152787-66-1, Promatrix 148969-98-6, Promatrix metalloproteinase-2 metalloproteinase-9 RL: BSU (Biological study, unclassified); BIOL (Biological study) (balance between synthesis of extracellular matrix components and their degradation by matrix metalloproteinases in basement membrane formation at dermal-epidermal junction) THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT RE (1) Amano, S; J Immunol Methods 1999, V224, P161 HCAPLUS (2) Bejarano, P; Biochem J 1988, V256, P413 HCAPLUS (3) Birkedal-Hansen, H; Curr Opin Cell Biol 1995, V7, P728 HCAPLUS (4) Brakebusch, C; EMBO J 2000, V19, P3990 HCAPLUS (5) Colognato, H; J Cell Biol 1999, V145, P619 HCAPLUS (6) De Arcangelis, A; J Cell Biol 1996, V133, P417 HCAPLUS

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L20 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
     2001:717824 HCAPLUS
AN
DN
     135:278068
ED
     Entered STN: 02 Oct 2001
ΤI
     Skin basement membrane formation promoters containing matrix
     metalloprotease inhibitors and manufacture of artificial skin using the
    promoters
IN
     Amano, Satoshi; Matsunaga, Yukiko; Inomata,
     Shinii
PA
     Shiseido Co., Ltd., Japan
SO
     Jpn. Kokai Tokkyo Koho, 17 pp.
     CODEN: JKXXAF
DT
     Patent
LΑ
     Japanese
IC
     ICM A61L027-00
     ICS A61K045-00; A61K045-06; A61P017-00
CC
     63-7 (Pharmaceuticals)
     Section cross-reference(s): 62
FAN.CNT 1
    PATENT NO.
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                               DATE
                                           APPLICATION NO.
                                                                 DATE
PΙ
    JP 2001269398
                         A2
                               20011002
                                           JP 2000-87574
                                                                  20000327
                         A1
                                           WO 2001-JP2507
     WO 2001072347
                               20011004
                                                                  20010327
        W: CN, KR, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
            PT, SE, TR
                         A1
                               20020220
                                           EP 2001-915860
     EP 1180371
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
    US 2002193875
                         A1
                               20021219
                                           US 2001-979712
                                                                  20011126
    US`2004038859
                                           US 2003-648485
                         A1
                               20040226
                                                                  20030827
PRAI JP 2000-87574
                         A
                               20000327
    WO 2001-JP2507
                         W
                               20010327
    US 2001-979712
                         A1
                               20011126
CLASS
                CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
                       _____
 JP 2001269398
                ICM
                       A61L027-00
                       A61K045-00; A61K045-06; A61P017-00
                ICS
 WO 2001072347
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                       A61K007/48; A61K007/48C22; A61K031/00+A; A61K038/55;
                       A61K045/06; A61L027/54; A61L027/60
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EP 1180371
 US 2002193875
                NCL
                       623/005.120; 424/439.000
                ECLA
                       A61K007/48; A61K007/48C22; A61K031/00+A; A61K038/55;
                       A61K045/06; A61L027/22; A61L027/54; A61L027/60
                NCL
US 2004038859
                       514/001.000
                ECLA
                       A61K007/48; A61K008/64; A61K031/00+A; A61K038/55;
                       A61K045/06; A61L027/22; A61L027/54; A61L027/60
    Skin basement membrane formation promoters and artificial skin formation
AB
    promoters contain matrix metalloprotease inhibitors and optionally matrix
    protein production promoters. Artificial skin is manufactured by adding matrix
    metalloprotease inhibitors and optionally matrix protein production promoters
    to a medium for artificial skin manufacture A skin model having stratified
     epidermis, obtained by culturing human foreskin-derived epidermal
    keratinocyte on contracted collagen gel, was further cultured in a medium
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Gitomer 10 / 648485 containing CGS 27023A for 2 wk to form basement membrane structure. Plant exts., e.g those of Thymus serpyllum, Potentilla tormentilla, Thea sinensis, etc., had a similar effect. Cosmetic formulations containing the basement membrane formation promoters were also skin basement membrane formation promoter matrix metalloprotease inhibitor; protein matrix prodn promoter skin basement membrane formation; artificial skin manuf matrix metalloprotease inhibitor Skin (artificial; skin basement membrane formation promoters containing matrix metalloprotease inhibitors and optionally matrix protein production promoters for manufacture of artificial skin) Proteins, specific or class RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative) (matrix, production promoters for; skin basement membrane formation promoters containing matrix metalloprotease inhibitors and optionally matrix protein production promoters for manufacture of artificial skin) Basement membrane (skin basement membrane formation promoters containing matrix metalloprotease inhibitors and optionally matrix protein production promoters for manufacture of artificial skin) Collagens, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (skin basement membrane formation promoters containing matrix metalloprotease inhibitors and optionally matrix protein production promoters for manufacture of artificial skin) Lysophosphatidylcholines RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (soybean; skin basement membrane formation promoters containing matrix metalloprotease inhibitors for manufacture of artificial skin) Transforming growth factors RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (α-; skin basement membrane formation promoters containing matrix metalloprotease inhibitors for manufacture of artificial skin)

IT Transforming growth factors
PL: BAC (Biological activity

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

 $(\beta 1-;$ skin basement membrane formation promoters containing matrix metalloprotease inhibitors for manufacture of artificial skin) 141907-41-7

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; skin basement membrane formation promoters containing matrix
metalloprotease inhibitors and optionally matrix protein production
promoters for manufacture of artificial skin)

IT 124168-73-6 169799-04-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(skin basement membrane formation promoters containing matrix metalloprotease inhibitors and optionally matrix protein production promoters for manufacture of artificial skin)

IT 169799-04-6

ST

IT

IT

IT

ΙT

IT

IT

TT

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(skin basement membrane formation promoters containing matrix metalloprotease inhibitors and optionally matrix protein production promoters for manufacture of artificial skin)

RN 169799-04-6 HCAPLUS

CN Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-

pyridinylmethyl)amino]-3-methyl-, monohydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

HCl

es d all bitestr 130 tot

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ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
L30
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2005:451248 HCAPLUS AN

DN142:487654

Entered STN: 27 May 2005 ED

- Polymer-containing intravascular devices for delivery of fibrosis-inducing ΤI
- Hunter, William L.; Gravett, David M.; Toleikis, Philip M.; Maiti, Arpita; IN Signore, Pierre E.; Liggins, Richard T.; Guan, Dechi
- PA Angiotech International A.-G., Switz.

PCT Int. Appl., 541 pp. SO

CODEN: PIXXD2

DTPatent

LА English

IC

ICM A61L027-00 ICS A61L027-54; A61L031-00; A61L031-16

63-7 (Pharmaceuticals) CC

EAN CAPP 14

FAN.CNT 14 PATENT NO.					KIND DATE		APPLICATION NO.						DATE					
PI	PI WO 2005046747			A2	A2 20050526			WO 2004-US38247						20041110				
		W :						AU,										
				•		•	•	DE,	•	•	•							
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								LV,										
			NO,	ΝZ,	OM,	PG,	PH,	ΡL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	sĸ,	SL,	SY,
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			NE,	SN,	TD,	TG												
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	US :	2005143817			A1		20050630			US 2004-6899					20041207			
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	US :	2005	1476	43		A1		2005	0707		US 2	004-	6893			2	0041	207

Search done by Noble Jarrell

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US 2005158274
                                20050721
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                          A1
PRAI US 2003-518785P
                                20031110
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    US 2003-523908P
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    US 2004-586861P
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                                20031203
     US 2004-986230
                          A1
                                20041110
    US 2004-986231
                         A1
                                20041110
CLASS
                CLASS PATENT FAMILY CLASSIFICATION CODES
PATENT NO.
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 WO 2005046747
                ICM
                       A61L027-00
                ICS
                       A61L027-54; A61L031-00; A61L031-16
                ECLA
WO 2005046747
                       A61B017/11; A61B017/12P
US 2005149158
                NCL
                        607/119.000
US 2005142163
                NCL
                        424/423.000
                       424/423.000; 623/016.110
US 2005169958
                NCL
                        424/423.000; 623/016.110
 US 2005169959
                NCL
US 2005143817
                        623/011.110; 623/926.000
                NCL
                        424/009.500; 424/423.000; 514/012.000; 514/027.000; 424/649.000; 514/283.000; 514/251.000; 514/575.000
US 2005147562
                NCL
                        424/094.630; 514/049.000; 514/251.000
 US 2005147599
                NCL
US 2005147643
                NCL
                        424/423.000; 514/012.000; 514/034.000; 514/283.000;
                        514/027.000; 514/251.000
                        424/078.380; 514/034.000; 514/055.000; 514/049.000;
US 2005158274
                NCL
                        514/251.000; 514/269.000
     The present invention provides compns. for delivery of selected
AΒ
     therapeutic agents via intravascular devices, as well as methods for
    making and using these devices to induce fibrotic response in the arterial
    wall. Within one aspect of the invention, drug-coated or drug-impregnated
     stent grafts and aneurysm coils are provided which induce adhesion or
     fibrosis in the surrounding tissue, or facilitate "anchoring" of the
     device/implant in situ, thus enhancing the efficacy. In other aspects,
     compns. that include fibrosis-inducing agents for use in embolizing and/or
     occluding aneurysms are described. Within various embodiments, fibrosis
     is induced by local or systemic release of specific pharmacol. agents that
     become localized to the adjacent tissue. For example, a flexible ring of
     fibronectin or poly(L-Lysine) was deposited on both ends of a covered
     stainless steel stent without compromise of the phys. characteristics of
     the covered stent. Also, silk braid (Ethicon, 4-0) was dip coated with
    poly(lactide-co-glycolide) (PLGA) and cyclosporine A. The cyclosporine
     A-loaded silk braid was dried and then attached to a polyurethane film by
    pressing the film/braids in a heat press for about 10 s such that the
     coated braid was embedded in the polyurethane film.
ST
     polymer vascular implant adhesion embolization fibrosis vascular disease
IT
    Drugs
        (Biolimus; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
IT
     Imaging agents
        (NMR contrast; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
IT
        (abdominal aortic; intravascular devices for delivery of
        fibrosis-inducing agents for treatment of vascular disease)
IT
   · Imaging agents
        (acoustic imaging contrast agents; intravascular devices for delivery
        of fibrosis-inducing agents for treatment of vascular disease)
IT
     Quaternary ammonium compounds, biological studies
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (alkylbenzyldimethyl, chlorides, complex with heparin; intravascular
        devices for delivery of fibrosis-inducing agents for treatment of
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vascular disease)

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IT
    Artery, disease
        (aorta; intravascular devices for delivery of fibrosis-inducing agents
        for treatment of vascular disease)
IT
    Medical goods
        (balloons; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
IT
     Polymers, biological studies
     Polyoxyalkylenes, biological studies
    RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (block; intravascular devices for delivery of fibrosis-inducing agents
        for treatment of vascular disease)
IT
    Medical goods
        (catheters; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
TT
    Polymers, biological studies
    RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (co-; intravascular devices for delivery of fibrosis-inducing agents
        for treatment of vascular disease)
IT
     Imaging agents
        (contrast, radiog.; intravascular devices for delivery of
        fibrosis-inducing agents for treatment of vascular disease)
IT
     Imaging agents
        (contrast; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
ΙT
     Polyesters, biological studies
    RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (dilactone-based; intravascular devices for delivery of
        fibrosis-inducing agents for treatment of vascular disease)
    Embolism
TT
        (embolization; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
TТ
    Animal tissue
        (engineering; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
IT
    Chelating agents
        (gadolinium; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
    Drug delivery systems
IT
        (gels; intravascular devices for delivery of fibrosis-inducing agents
        for treatment of vascular disease)
IT
        (iliac aortic; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
IT
     Prosthetic materials and Prosthetics
        (implants, intravascular; intravascular devices for delivery of
        fibrosis-inducing agents for treatment of vascular disease)
IT
     Cytokines
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (inhibitors; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
IT
    Drug delivery systems
        (injections; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
IT
    Adhesives
    Aneurysm
    Anti-infective agents
    Anti-inflammatory agents
    Anticoagulants
    Artery, disease
    Blood vessel, disease
     Coating materials
     Coloring materials
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Dyes
    Fibrosis
    Human
    Hydrogels
    Immunosuppressants
    Pigments, nonbiological
    Silk
        (intravascular devices for delivery of fibrosis-inducing agents for
        treatment of vascular disease)
TТ
    Anthracyclines
       Collagens, biological studies
    Fibrinogens
    Fibrins
    Fibronectins
    Fluoropolymers, biological studies
    Growth factors, animal
    Interleukin 1
    Interleukin 6
    Interleukin 8
    Macromonomers
    Metals, biological studies
    Polyanhydrides
    Polyesters, biological studies
    Polymers, biological studies
    Polyoxyalkylenes, biological studies
    Polysiloxanes, biological studies
    Polyurethanes, biological studies
    RGD peptides
    Silicates, biological studies
    Synthetic rubber, biological studies
    Tumor necrosis factors
    RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
    study); USES (Uses)
        (intravascular devices for delivery of fibrosis-inducing agents for
        treatment of vascular disease)
IT
    Drug delivery systems
        (liqs.; intravascular devices for delivery of fibrosis-inducing agents
        for treatment of vascular disease)
IT
    Drug delivery systems
        (micelles; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
TT
    Drug delivery systems
        (microspheres; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
    Particles
TΤ
        (mineral; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
TΤ
    Drug delivery systems
        (nanospheres; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
TТ
    Minerals, biological studies
    RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
    study); USES (Uses)
        (particles; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
TΤ
    Drug delivery systems
        (pastes; intravascular devices for delivery of fibrosis-inducing agents
        for treatment of vascular disease)
TT
    Urethane rubber, biological studies
    RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (polycarbonate-; intravascular devices for delivery of
        fibrosis-inducing agents for treatment of vascular disease)
IT
    Synthetic rubber, biological studies
    RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
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(polycarbonate-polyurethane; intravascular devices for delivery of
        fibrosis-inducing agents for treatment of vascular disease)
    Polyoxyalkylenes, biological studies
ΤТ
    RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (polyester-, block; intravascular devices for delivery of
        fibrosis-inducing agents for treatment of vascular disease)
TΤ
    Hydrocarbons, biological studies
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (polymers; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
IΤ
     Polyesters, biological studies
    RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (polyoxyalkylene-, block; intravascular devices for delivery of
        fibrosis-inducing agents for treatment of vascular disease)
IΤ
    Cytokines
    RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
    study); USES (Uses)
        (proinflammatory; intravascular devices for delivery of
        fibrosis-inducing agents for treatment of vascular disease)
ΙT
    Fibroblast
        (promotion of migration and proliferation of; intravascular devices for
        delivery of fibrosis-inducing agents for treatment of vascular disease)
ΙT
    Adhesion, biological
    Angiogenesis
    Cell migration
    Cell proliferation
     Extracellular matrix
    Regeneration, animal
        (promotion of; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
IΤ
    Platelet-derived growth factors
    RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (recombinant human; intravascular devices for delivery of
        fibrosis-inducing agents for treatment of vascular disease)
IT
    Artery, disease
        (restenosis, inhibitors; intravascular devices for delivery of
        fibrosis-inducing agents for treatment of vascular disease)
IT
    Medical goods
        (shunts; intravascular devices for delivery of fibrosis-inducing agents
        for treatment of vascular disease)
IT
    Drug delivery systems
        (solns.; intravascular devices for delivery of fibrosis-inducing agents
        for treatment of vascular disease)
    Medical goods
IT
        (stents; intravascular devices for delivery of fibrosis-inducing agents
        for treatment of vascular disease)
ΙT
    Drug delivery systems
        (sustained-release; intravascular devices for delivery of
        fibrosis-inducing agents for treatment of vascular disease)
IT
    Medical goods
        (sutures; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
IT
    Aneurysm
        (thoracic aortic; intravascular devices for delivery of
        fibrosis-inducing agents for treatment of vascular disease)
IT
    Engineering
        (tissue; intravascular devices for delivery of fibrosis-inducing agents
        for treatment of vascular disease)
IT
    Medical goods
        (tubes; intravascular devices for delivery of fibrosis-inducing agents
        for treatment of vascular disease)
IT
    Medical goods
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(wires, coronary infusion guide wires; intravascular devices for
        delivery of fibrosis-inducing agents for treatment of vascular disease)
IT
     Transforming growth factors
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (β-; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
IT
     61912-98-9. IGF
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (A; intravascular devices for delivery of fibrosis-inducing agents for
        treatment of vascular disease)
     11128-99-7, Angiotensin II
ΙT
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (PEG-encapsulated; intravascular devices for delivery of
        fibrosis-inducing agents for treatment of vascular disease)
IT
     15802-18-3D, Cyanoacrylic acid, derivs.
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (adhesives; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
IT
     59-30-3, Folic acid, biological studies
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (antagonists; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
тт
     7440-54-2, Gadolinium, biological studies
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (chelates; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
ΙT
     17031-92-4, Calcium pyrophosphate dihydrate
                                                    59216-10-3, Monosodium urate
     monohydrate
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (inflammatory microcrystals; intravascular devices for delivery of
        fibrosis-inducing agents for treatment of vascular disease)
IT
     9028-93-7, Inosine 5'-monophosphate dehydrogenase 141907-41-7
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (inhibitors; intravascular devices for delivery of fibrosis-inducing
        agents for treatment of vascular disease)
IT
     50-02-2, Dexamethasone 50-24-8, Prednisolone
                                                       50-28-2,
     Estra-1,3,5(10)-triene-3,17-diol (17\beta)-, biological studies
     50-53-3, Chlorpromazine, biological studies 50-76-0, Actinomycin D
     50-78-2, Aspirin 51-21-8, 5-Fluorouracil 53-03-2, Prednisone
     53-06-5, Cortisone 56-53-1, Diethylstilbestrol 57-22-7, Vincristine 58-32-2, Dipyridamole 59-05-2, Methotrexate 60-54-8, Tetracycline
     64-17-5, Ethanol, biological studies 74-79-3, L-Arginine, biological
     studies 79-10-7D, Acrylic acid, polymers 83-43-2, 6\alpha-
     Methylprednisolone 100-42-5D, Styrene, polymers 106-99-0D, Butadiene,
     polymers 115-11-7D, Isobutylene, polymers 124-94-7, Triamcinolone
     127-07-1D, Hydroxyurea, derivs. 127-31-1, Fludrocortisone
     all-trans-Retinoic acid 378-44-9, Betamethasone 518-28-5,
     Podophyllotoxin 564-25-0, Doxycycline
                                               1304-56-9, Beryllium oxide,
                         1332-37-2, Iron oxide, biological studies
     biological studies
     4005-51-0, Aminothiadiazole 4759-48-2, Isotretinoin
                                                             7439-89-6. Iron.
     biological studies 7439-95-4, Magnesium, biological studies
    7440-06-4D, Platinum, complexes 7440-25-7, Tantalum, biological studies 7440-26-8, Technetium, biological studies 7440-39-3, Barium, biological
              7440-39-3D, Barium, compds. 7440-41-7, Beryllium, biological
               7440-47-3, Chromium, biological studies 7440-50-8, Copper,
     studies
     biological studies 7631-86-9, Silica, biological studies
                   9002-72-6, Growth hormone 9002-84-0,
     Camptothecin
     Polytetrafluoroethylene 9003-07-0, Polypropylene 9003-27-4,
     Polyisobutylene 9003-53-6, Polystyrene 9003-63-8, Poly(butyl
     methacrylate) 9004-61-9, Hyaluronic acid 9004-74-4,
     Methoxypolyethylene glycol 9005-49-6, Heparin, biological studies
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9005-49-6D, Heparin, complex with benzalkonium chloride
                                                         9012-76-4,
Chitosan 9061-61-4, Nerve growth factor 9067-32-7D, Sodium
hyaluronate, crosslinked 10102-43-9, Nitric oxide, biological studies
10118-90-8, Minocycline 11056-06-7, Bleomycin 12597-68-1, Stainless
steel, biological studies 14110-64-6, Cytochalasin A 14807-96-6, Talc,
biological studies 14808-60-7, Quartz, biological studies 15663-27-1,
           22260-51-1, Bromocriptine mesylate 23214-92-8, Doxorubicin
24280-93-1, Mycophenolic acid 24937-78-8, Poly(ethylene-vinyl acetate)
25067-34-9, Ethylene-vinyl alcohol copolymer 25104-18-1, Poly(L-lysine)
25322-68-3, Polyethylene glycol
                                26780-50-7, Glycolide-lactide copolymer
32222-06-3, 1\alpha, 25-Dihydroxyvitamin D3 33069-62-4, Paclitaxel
33419-42-0, Etoposide 36791-04-5, Ribavirin 38000-06-5, Poly(L-lysine)
42503-45-7D, tetrasulfhydryl derivative 53123-88-9, Sirolimus 53902-12-8,
Tranilast 55837-20-2, Halofuginone 59865-13-3, Cyclosporin A
60084-10-8, Tiazofurin 62031-54-3, Fibroblast growth factor
65271-80-9, Mitoxantrone
                         79902-63-9, Simvastatin
                                                  83869-56-1. GM-CSF
84238-67-5, Mercox 86102-31-0, TIMP proteinase inhibitor 87771-40-2,
            106096-93-9, BFGF 108736-35-2, Angiopeptin
Optiray 320
Viramidine
            125265-78-3, N-Carboxybutyl chitosan 127464-60-2, VEGF
130370-60-4, Batimastat 145599-86-6, Cerivastatin 154039-60-8,
Marimastat 159351-69-6, Everolimus
                                     161407-67-6, Thiophenfurin
169501-65-9 169799-04-6, CGS 27023A
185681-64-5, QP 2 189460-40-0, Connective tissue growth factor
193022-04-7, Ro 1130830 207986-05-8, Glycolide-lactide-polyethylene
                        221877-54-9, ABT 578 237080-85-2, Mercox CL 2B
glycol block copolymer
259188-38-0, BMS 275291 302781-03-9 365564-13-2, L-Lactide-
polyethylene glycol monomethyl ether block copolymer
                                                     852060-45-8, BCP
671 852060-49-2, Lantrunculin D
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
study); USES (Uses)
   (intravascular devices for delivery of fibrosis-inducing agents for
   treatment of vascular disease)
111-30-8, Glutaraldehyde
                          1892-57-5, 1-Ethyl-3-(3-
dimethylaminopropyl) carbodiimide
RL: RCT (Reactant); RACT (Reactant or reagent)
   (intravascular devices for delivery of fibrosis-inducing agents for
   treatment of vascular disease)
169799-04-6, CGS 27023A
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
study); USES (Uses).
   (intravascular devices for delivery of fibrosis-inducing agents for
   treatment of vascular disease)
169799-04-6 HCAPLUS
Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-
pyridinylmethyl)amino]-3-methyl-, monohydrochloride, (2R)- (9CI) (CA
INDEX NAME)
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Absolute stereochemistry.

IT

IT

RN

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L30 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2004:589450 HCAPLUS
DN
     141:128919
ED
     Entered STN: 23 Jul 2004
ΤI
     Compositions and methods of using Collajolie
     Hunter, William L.; Gravett, David M.; Toleikis, Philip M.; Maiti, Arpita
ΤN
PA
     Angiotech Pharmaceuticals, Inc., Can.
so
     PCT Int. Appl., 92 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
TC
     ICM A61L027-24
     ICS A61L027-12; A61K006-033; A61K038-39; A61K038-48; A61L027-60;
           A61F002-14; A61F002-10; A61F002-44
     63-7 (Pharmaceuticals)
CC
FAN.CNT 1
                                               APPLICATION NO.
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                           KIND DATE
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                           ´A2
     WO 2004060425
                                   20040722
                                             WO 2003-US41330
                                                                         20031224
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     WO 2004060425
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              LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
              OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
         TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
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                                                US 2003-746911
                                                                        20031224
     US 2004192658
                            A1
                                   20040930
                            P
                                   20021227
PRAI US 2002-436806P
CLASS
                  CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
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 WO 2004060425
                  ICM
                          A61L027-24
                          A61L027-12; A61K006-033; A61K038-39; A61K038-48;
                  ICS
                          A61L027-60; A61F002-14; A61F002-10; A61F002-44
                          A61K038/39+M; A61K038/57+M; A61L015/32A; A61L027/12;
 WO 2004060425
                  ECLA
                          A61L027/24; A61L027/46; A61L027/54; A61L027/60;
                          A61L031/04F2; A61L031/16
                          514/152.000; 424/094.100; 514/575.000
 US 2004192658
                  NCL
                  ECLA
                          A61K038/39+M; A61K038/57+M; A61L015/32A; A61L027/24;
                          A61L027/54; A61L031/04F2; A61L031/16
     MARPAT 141:128919
OS
     Compns. and devices comprising collagen and a compound that inhibits the
ΔB
     activity of metalloprotease (collagenase) to produce a collagen-based
     implant with enhanced durability in vivo (Collajolie) are described. The
     metalloprotease inhibitor is selected from a tissue inhibitor of matrix
     metalloprotease (TIMP), a tetracycline, a hydroxamate, a mercapro-based
     compound, or a bisphosphonate. The composition further comprises hydroxyapatite
     and biodegradable or non-biodegradable polymer, selected from albumin,
     gelatin, polysaccharides, fibrinogen, polyanhydrides, polyesters, etc.
     method for augmentation or repair of tissues, e.g., a bone, comprises using the compns. and implants made of them. For example, a freeze-dried
     Batimastat solid composition capable of forming micelles upon constitution with
     an aqueous collagen-containing medium was prepared To a clear liquid obtained by
     mixing 41.29 g of MePEG and 412.84 g of 60:40 MePEG/poly(DL-lactide)
     diblock copolymer at 75°, 45.87 g Batimastat in THF was added, and
     the mixture was solidified. A solid Batimastat-polymer matrix (327 g) was
     dissolved in the phosphate buffer (237.8 g of dibasic sodium phosphate
     heptahydrate, 15.18 g of monobasic sodium phosphate monohydrate in 1600 mL
     of water) and filled into vials with 15 mL aliquots and freeze dried. The
      freeze-dried micellar Batimastat material (40 mg) was weighed into a
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TT

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capped 1 mL syringe and sterilized. Just prior to application, the
plastic pouch containing the sterilized freeze-dried material was opened and
connected through a dual syringe connector to a syringe containing 2 mL 3.5%
bovine collagen (95% type I and 5% Type III), and the collagen material
was pushed into the syringe containing the micellar material to obtain a
homogeneous solution The material was then transferred into the syringe that
originally contained the collagen and the syringe was disconnected from
the connector.
collagen matrix collagenase inhibitor polymer Collajolie implant
Bone morphogenetic proteins
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
study); USES (Uses)
   (2; compns. containing collagen and metalloprotease inhibitor for implants)
Bone morphogenetic proteins
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
study); USES (Uses)
   (8; compns. containing collagen and metalloprotease inhibitor for implants)
Polycarbonates, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
study); USES (Uses)
   (aliphatic; compns. containing collagen and metalloprotease inhibitor for
   implants)
Intestine
   (anus, disease, incontinence, implants for management of; compns.
   containing collagen and metalloprotease inhibitor for implants)
Bone
   (artificial; compns. containing collagen and metalloprotease inhibitor for
   implants)
Bone
   (augmentation; compns. containing collagen and metalloprotease inhibitor
   for implants)
Polyesters, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
study); USES (Uses)
   (caprolactone-based; compns. containing collagen and metalloprotease
   inhibitor for implants)
Polymers, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
study); USES (Uses)
   (co-; compns. containing collagen and metalloprotease inhibitor for
   implants)
Skin
   (collagen production from; compns. containing collagen and metalloprotease
   inhibitor for implants)
Medical goods
   (colostomy bags, reinforcement of; compns. containing collagen and
   metalloprotease inhibitor for implants)
Wound healing promoters
   (compns. containing collagen and metalloprotease inhibitor for implants)
Albumins, biological studies
Biopolymers
Fibrinogens
  Gelatins, biological studies
Polyanhydrides
Polyesters, biological studies
Polymer blends
Polymers, biological studies
Polysaccharides, biological studies
Proteins
Silicone rubber, biological studies
Tetracyclines
Thiols, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
study); USES (Uses)
   (compns. containing collagen and metalloprotease inhibitor for implants)
```

```
IT
     Polyesters, biological studies
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (dilactone-based; compns. containing collagen and metalloprotease inhibitor
        for implants)
IT
     Medical goods
        (dressings; compns. containing collagen and metalloprotease inhibitor for
        implants)
     Digestive tract, disease
IT
        (gastroesophageal reflux, implants for management of; compns. containing
        collagen and metalloprotease inhibitor for implants)
TТ
     Polyesters, biological studies
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (glycolide-based; compns. containing collagen and metalloprotease inhibitor
        for implants)
IT
     Musculoskeletal diseases
        (hernia, repair; compns. containing collagen and metalloprotease inhibitor
        for implants)
TT
     Prosthetic materials and Prosthetics
        (implants, spinal disks; compns. containing collagen and metalloprotease
        inhibitor for implants)
TT
     Dental materials and appliances
        (implants; compns. containing collagen and metalloprotease inhibitor for
        implants)
IT
     Glaucoma (disease)
        (improvement of drainage in; compns. containing collagen and
        metalloprotease inhibitor for implants)
TT
     Spinal column
        (intervertebral disk, replacement of; compns. containing collagen and
        metalloprotease inhibitor for implants)
     Polyesters, biological studies
тт
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (lactide; compns. containing collagen and metalloprotease inhibitor for
        implants)
TT
     Drug delivery systems
        (liposomes; compns. containing collagen and metalloprotease inhibitor for
        implants)
IT
     Drug delivery systems
        (microspheres; compns. containing collagen and metalloprotease inhibitor
        for implants)
IT
     Polyethers, biological studies
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (ortho ester group-containing; compns. containing collagen and metalloprotease
     inhibitor for implants)
Polyoxyalkylenes, biological studies
IT
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (polyester-; compns. containing collagen and metalloprotease inhibitor for
        implants)
IT
     Polyesters, biological studies
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (polyoxyalkylene-; compns. containing collagen and metalloprotease
        inhibitor for implants)
IT
     Cartilage
     Ligament
     Tendon
        (repair; compns. containing collagen and metalloprotease inhibitor for
        implants)
IT
     Medical goods
        (sponges; compns. containing collagen and metalloprotease inhibitor for
        implants)
IT
     Cataract
```

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(surgery, corneal shield for; compns. containing collagen and
        metalloprotease inhibitor for implants)
TT
     Medical goods
        (sutures, line reinforcement; compns. containing collagen and
        metalloprotease inhibitor for implants)
IT
     Abdomen
        (tissue repair; compns. containing collagen and metalloprotease inhibitor
        for implants)
IT
     Periodontium, disease
        (treatment of; compns. containing collagen and metalloprotease inhibitor
        for implants)
IT
     Collagens, biological studies
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (type I; compns. containing collagen and metalloprotease inhibitor for
        implants)
IT
     Collagens, biological studies
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (type II; compns. containing collagen and metalloprotease inhibitor for
        implants)
IT
     Collagens, biological studies
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (type III; compns. containing collagen and metalloprotease inhibitor for
        implants)
IT
     Collagens, biological studies
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (type IV; compns. containing collagen and metalloprotease inhibitor for
        implants)
IT
     Thorax
        (wall repair; compns. containing collagen and metalloprotease inhibitor for
        implants)
ΙT
     9001-75-6, Pepsin
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (collagen production by skin degradation with; compns. containing collagen and
        metalloprotease inhibitor for implants)
IT
     60-54-8, Tetracycline 64-75-5, Tetracycline hydrochloride
                                                                    79-10-7D.
     Acrylic acid, derivs., polymers 79-0
polymers 1306-06-5, Hydroxyapatite
                                      79-41-4D, Methacrylic acid, derivs.,
                                            9002-89-5, Polyvinyl alcohol
     9003-11-6, Ethylene oxide-propylene oxide copolymer
                                                           9004-34-6,
     Cellulose, biological studies 9004-54-0, Dextran, biological studies
     9005-25-8, Starch, biological studies
                                             10118-90-8, Minocycline
                                             13598-36-2D, Phosphonic acid,
     10592-13-9, Doxycycline hydrochloride
     alkylidenebis- derivs. 13614-98-7, Minocycline hydrochloride
     24937-78-8, Ethylene-vinyl acetate copolymer 24980-41-4,
     Poly(s-caprolactone) 25248-42-4, Poly[oxy(1-oxo-1,6-hexanediyl)]
     26009-03-0, Polyglycolide 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-
                    26063-00-3, Poly(hydroxybutyrate)
     ethanediyl)]
                                                       26202-08-4,
     Polyglycolide
                    26680-10-4, Poly(DL-lactide) 26744-04-7
                                                                  26780-50-7.
     Poly(DL-lactide-co-glycolide)
                                    85087-20-3, Doxycline
                                                             124861-55-8,
     TIMP-2
              130370-60-4, Batimastat 140208-24-8, TIMP-1
                                                               145809-21-8,
             154039-60-8, Marimastat 169799-04-6, CGS
     TIMP-3
             186207-03-4, TIMP-4
                                    190648-49-8, Trocade
                                                           193022-04-7,
     Ro 1130830
                 259188-38-0, BMS 275291
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (compns. containing collagen and metalloprotease inhibitor for implants)
IT
     188360-48-7, DL-Lactide-methoxy-poly(ethylene glycol) block copolymer
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (diblock; compns. containing collagen and metalloprotease inhibitor for
        implants)
IΤ
     9001-12-1, Collagenase
                             69494-91-3, Maturase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
```

(inhibitors; compns. containing collagen and metalloprotease inhibitor for implants)

IT 169799-04-6, CGS 27023A

RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(compns. containing collagen and metalloprotease inhibitor for implants)

RN 169799-04-6 HCAPLUS

CN Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3 pyridinylmethyl)amino]-3-methyl-, monohydrochloride, (2R)- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.

HCl

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L30 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
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AN 2004:513327 HCAPLUS

DN 141:65136

ED Entered STN: 25 Jun 2004

TI Method of using a COX-2 inhibitor and a TACE inhibitor as a combination therapy for the treatment of neoplasia, pain, inflammation, and vaso-occlusive events

IN Masferrer, Jaime L.; Stephenson, Diane T.

PA Pharmacia Corporation, USA

SO U.S. Pat. Appl. Publ., 143 pp., Cont.-in-part of U.S. Ser. No. 868,063. CODEN: USXXCO

DT Patent

LA English

IC ICM A61K031-50

ICS A61K031-415; A61K031-195

INCL 514247000; 514567000; 514406000; 514471000

CC 1-12 (Pharmacology)

Section cross-reference(s): 63

FAN.CNT 21

FAN.	CNT	21																			
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PI	US 2004122011					A1		20040624			US 2003-423526						20030425 <				
	ΕP	1522		A1 20050413			EP 2004-26577						19991222 <								
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			ΙE,	FI,	RO,	CY															
	WO	O 2004096206				A2 20041111					WO 2004-US12620						20040423				
	WO	2004096206				A3 2			20050407			•									
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			NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,			
			ТJ,	TM,	TN,	TR,	TT,	TZ,	UΑ,	ŪĠ,	US,	υZ,	VC,	VN,	¥U,	ZA,	ZM,	ZW			
		RW:	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,			

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BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
             SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
             TD, TG
PRAI US 1998-113786P
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                                19991222
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     US 2001-868063
                          A2
                                20011005
     US 1999-385214
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                                19990827
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     EP 1999-968939
                          A3
                                19991222
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     US 2003-423526
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                                20030425
CLASS
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                 CLASS PATENT FAMILY CLASSIFICATION CODES
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US 2004122011
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                 TCM
                 ICS
                        A61K031-415; A61K031-195
                        514247000; 514567000; 514406000; 514471000
                 INCL
                 NCL
                        514/247.000; 514/567.000; 514/406.000; 514/471.000
US 2004122011
                        A61K031/135+M; A61K031/415; A61K031/415+M; A61K031/42;
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                        A61K031/42+M; A61K031/445+M; A61K031/505;
                        A61K031/505+M; A61K031/506; A61K031/506+M;
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                        A61K045/06; A61K045/06+M
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                        A61K031/135+M; A61K031/415+M; A61K031/42+M;
EP 1522313
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                        A61K031/675+M; A61K033/24+M; A61K041/00; A61K045/06 <--
WO 2004096206
                ECLA
                        A61K045/06
os
     MARPAT 141:65136
AB
     The present invention provides compns. and methods to treat, prevent, or
     inhibit a neoplasia, a neoplasia-related disorder, pain, inflammation, an
     inflammatory-related disorder, a vaso-occlusive event or a
     vaso-occlusive-related disorder in a mammal using a combination of a COX-2
     inhibitor and a TACE inhibitor.
ST
     cyclooxygenase 2 TACE inhibitor combination therapeutic; antitumor
     antiinflammatory analgesic cyclooxygenase 2 TACE inhibitor combination;
     vasoocclusive event treatment cyclooxygenase 2 TACE inhibitor combination
TΤ
     Reproductive organ
        (Bartholin's gland, carcinoma; COX-2 inhibitor-TACE inhibitor
        combination for treatment of neoplasia, pain, inflammation, and
        vaso-occlusive events)
IT
        (Bartholin's, carcinoma; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
ΙT
     Acne
     Adenoma
     Allergy
     Allergy inhibitors
     Alzheimer's disease
     Analgesics
     Anemia (disease)
     Aneurysm
     Angiogenesis
     Angiogenesis inhibitors
     Anti-Alzheimer's agents
     Anti-inflammatory agents
     Anti-ischemic agents
     Antiarteriosclerotics
     Antiarthritics
     Antiasthmatics
     Antidepressants
     Antidiabetic agents
     Antiparkinsonian agents
     Antipyretics
     Antirheumatic agents
     Antitumor agents
     Antiulcer agents
     Apoptosis
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Arteriosclerosis Arthritis Asthma Atherosclerosis Autoimmune disease Behcet's syndrome Biliary tract, neoplasm Bladder, neoplasm Blood coaquiation Blood vessel, disease Bone, neoplasm Brain, neoplasm Bronchi, neoplasm Burn Cachexia Carcinoid Carcinoma Carcinoma Cardiovascular agents Cognition enhancers Common cold Cyst, pathological Cystic fibrosis Dermatitis Dermatomyositis Diabetes mellitus Digestive tract, neoplasm Drug delivery systems Dysmenorrhea Eczema Embolism Emphysema Endocrine system, neoplasm Esophagus, neoplasm Eye, disease Fever and Hyperthermia Gallbladder, neoplasm Gastrointestinal agents Gout Headache Hemophilia Hepatitis Hodgkin's disease Immunodeficiency Immunomodulators Inflammation Kidney, disease Kidney, neoplasm Larynx, neoplasm Leukemia Leukemia, acute myeloid Liver, disease Liver, neoplasm Lung, neoplasm Lymphoma Mammary gland, neoplasm Melanoma Mouth, neoplasm Multiple myeloma Multiple sclerosis Myasthenia gravis Myositis Neoplasm Nervous system, neoplasm Nervous system agents Nose, neoplasm

Osteoarthritis Osteoporosis Ovary, neoplasm Pain Pancreas, neoplasm Parkinson's disease Periodontium, disease Pharynx, neoplasm Pituitary gland, neoplasm Prostate gland, neoplasm Psoriasis Respiratory distress syndrome Respiratory tract, neoplasm Rheumatic fever Rheumatoid arthritis Sarcoidosis Sarcoma Sepsis Sjogren's syndrome Skin, disease Skin, neoplasm Stomach, neoplasm Testis, neoplasm Thrombosis Thyroid gland, neoplasm Tongue, neoplasm Urinary tract, neoplasm Uterus, neoplasm Wound Wound healing promoters (COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Anticoagulants Platelet aggregation inhibitors Thrombolytics (COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events, and use with other agents) Corticosteroids, biological studies RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events, and use with other agents) Chlamydia (Chlamydia-induced inflammation; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Inflammation (Crohn's disease; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Intestine, disease (Crohn's; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Bone, neoplasm (Ewing's sarcoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT . Sarcoma (Ewing's; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Nervous system, disease (Huntington's chorea; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Sarcoma (Kaposi's; COX-2 inhibitor-TACE inhibitor combination for treatment of

TТ

TT

IT

TT

TT

IT

IT

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neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Blood vessel, disease
        (Raynaud's phenomenon; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Arthritis
        (Reiter's syndrome; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
TT
    Leukemia
        (T-cell; COX-2 inhibitor-TACE inhibitor combination for treatment of
       neoplasia, pain, inflammation, and vaso-occlusive events)
    UV radiation
IT
        (UV damage; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Neoplasm
        (VIPoma; COX-2 inhibitor-TACE inhibitor combination for treatment of
       neoplasia, pain, inflammation, and vaso-occlusive events)
TT
     Granulomatous disease
        (Wegener's granulomatosis; COX-2 inhibitor-TACE inhibitor combination
        for treatment of neoplasia, pain, inflammation, and vaso-occlusive
        events)
IT
     Intestine, disease
        (Whipple's; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Kidney, neoplasm
        (Wilms'; COX-2 inhibitor-TACE inhibitor combination for treatment of
       neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Keratosis
        (actinic; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Leukemia
        (acute lymphocytic; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Respiratory distress syndrome
        (acute; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
TТ
     Carcinoma
        (adenocarcinoma, neuroepithelial; COX-2 inhibitor-TACE inhibitor
        combination for treatment of neoplasia, pain, inflammation, and
        vaso-occlusive events)
IT
        (adenocarcinoma, papillary serous; COX-2 inhibitor-TACE inhibitor
        combination for treatment of neoplasia, pain, inflammation, and
        vaso-occlusive events)
IT
     Carcinoma
        (adenocarcinoma; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Carcinoma
        (adenoid cystic; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Liver, neoplasm
        (adenoma; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IT
        (adenosarcoma; COX-2 inhibitor-TACE inhibitor combination for treatment
        of neoplasia, pain, inflammation, and vaso-occlusive events)
ΙT
        (adenosquamous; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Allergy
     Inflammation
     Nerve, disease
        (allergic neuritis; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Allergy
     Inflammation
     Nose, disease
```

(allergic rhinitis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TT Disease, animal (amaurosis fugax; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TT Brain, disease (amyloid angiopathy; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Nervous system, disease (amyotrophic lateral sclerosis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Heart, disease IT (angina pectoris, unstable; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Heart, disease (angina pectoris; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Surgery (angioplasty, inflammation; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Inflammation Spinal column, disease (ankylosing spondylitis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Antiarteriosclerotics (antiatherosclerotics; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Intestine TТ (anus, anal cancer; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Artery, disease (aorta, stenosis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) ΙT (aortic; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Anemia (disease) (aplastic; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Blood vessel (artificial, inflammation; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Joint, anatomical (artificial, loosening of artificial joint implants; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Neuroglia, neoplasm (astrocytoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Infection (bacterial, bacterial-induced inflammation; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Skin, neoplasm (basal cell carcinoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT'Carcinoma (basal cell; COX-2 inhibitor-TACE inhibitor combination for treatment

(benign hyperplasia; COX-2 inhibitor-TACE inhibitor combination for

of neoplasia, pain, inflammation, and vaso-occlusive events)

IT

Prostate gland, disease

```
treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Hyperplasia
        (benign prostatic; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Biliary tract, neoplasm
        (bile duct, intrahepatic; COX-2 inhibitor-TACE inhibitor combination
        for treatment of neoplasia, pain, inflammation, and vaso-occlusive
        events)
IT
     Neoplasm
        (blastoma, hemangioblastoma; COX-2 inhibitor-TACE inhibitor combination
        for treatment of neoplasia, pain, inflammation, and vaso-occlusive
        events)
IT
     Neoplasm
        (bone marrow; COX-2 inhibitor-TACE inhibitor combination for treatment
        of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
        (bronchial; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
TТ
     Bronchi, disease
     Inflammation
        (bronchitis; COX-2 inhibitor-TACE inhibitor combination for treatment
        of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Joint, anatomical
        (bursa, bursitis; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Neoplasm.
        (cancer pain; COX-2 inhibitor-TACE inhibitor combination for treatment
        of neoplasia, pain, inflammation, and vaso-occlusive events)
ΙT
     Biliary tract, disease
     Connective tissue, disease
     Heart, disease
     Joint, anatomical
     Muscle, disease
     Penis
     Ureter
     Urethra
     Vagina, disease
        (cancer; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
     Bronchi, neoplasm
        (carcinoma; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
ΙT
        (carcinosarcoma; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Heart, disease
        (cardiac stenosis; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Ischemia
        (cardiac; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Nervous system, disease
        (central; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
TΤ
     Edema
     Ischemia
        (cerebral; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Uterus, neoplasm
        (cervix; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
ΙT
     Carcinoma
        (cholangiocarcinoma; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Biliary tract, neoplasm
        (cholangioma; COX-2 inhibitor-TACE inhibitor combination for treatment
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of neoplasia, pain, inflammation, and vaso-occlusive events) ITSarcoma (chondosarcoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Brain, neoplasm Meninges (choroid plexus carcinoma, choroid plexus papilloma/carcinoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Papilloma (choroid plexus papilloma/carcinoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Carcinoma (choroid plexus, choroid plexus papilloma/carcinoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TΤ (chronic lymphocytic; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Leukemia (chronic myelocytic; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TT Lung, disease (chronic obstructive; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Mental disorder (cognitive; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Intestine, neoplasm IT (colon; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Intestine, neoplasm (colorectal; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) ΙT Eye, disease Inflammation (conjunctivitis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Dermatitis (contact; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Eye, disease (cornea, injury; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Injury (corneal; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Surgery (coronary artery bypass; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TΤ Heart, disease (coronary plaque inflammation; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Artery (coronary, bypass surgery; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TΤ Artery, disease (coronary, stenosis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TT Artery, disease (coronary; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events)

Adenoma

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(cystadenoma; COX-2 inhibitor-TACE inhibitor combination for treatment
        of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Nerve, disease
        (degeneration; COX-2 inhibitor-TACE inhibitor combination for treatment
        of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Mental disorder
        (dementia, alc.; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Mental disorder
        (dementia, cortical; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Mental disorder
        (dementia, multi-infarct; COX-2 inhibitor-TACE inhibitor combination
        for treatment of neoplasia, pain, inflammation, and vaso-occlusive
        events)
IT
     Mental disorder
        (dementia, vascular; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Pain
        (dental; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Mental disorder
        (depression; COX-2 inhibitor-TACE inhibitor combination for treatment
        of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Hemorrhage
        (digestive tract; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
TT
     Meninges
        (disease, cancer; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
TΤ
     Tendon
        (disease, tendinitis; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Neuromuscular junction
        (disease; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Cognition
     Reproduction, animal
        (disorder; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Inflammation
     Intestine, disease
        (diverticulitis; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IΤ
     Intestine, neoplasm
        (duodenum; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
     Brain, disease
TT
        (edema; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IT
        (endarterectomy inflammation; COX-2 inhibitor-TACE inhibitor
        combination for treatment of neoplasia, pain, inflammation, and
        vaso-occlusive events)
IT
     Neoplasm
        (endodermal sinus tumor; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Sarcoma
        (endometrial stromal; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Hyperplasia
        (endometrial; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Uterus, disease
        (endometriosis; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
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IT Uterus, neoplasm (endometrium, adenocarcinoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Uterus, disease (endometrium, hyperplasia; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) ΙT Endothelium (endothelial cell cancer; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Blood vessel, neoplasm (endothelioma, hemangioendothelioma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TТ Eosinophilia (eosinophilia-myalgia syndrome; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Brain, neoplasm (ependymoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TT Skin, disease (epidermolysis bullosa; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Eye, disease (eye and orbit cancer; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Heart, disease (failure; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Amyloidosis (familial Mediterranean fever; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Fever and Hyperthermia IT (familial Mediterranean; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TT Eosinophilia (fasciitis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Reproductive tract TT (female, cancer; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Hyperplasia IT(focal nodular; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Neoplasm (gastrinoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Inflammation Stomach, disease (gastritis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TΤ Neoplasm (germ cell; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Gingiva, disease Inflammation (gingivitis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events)

(glioblastoma; COX-2 inhibitor-TACE inhibitor combination for treatment

of neoplasia, pain, inflammation, and vaso-occlusive events)

IT

ΙT

Neuroglia, neoplasm

Pancreatic islet of Langerhans, neoplasm

(glucagonoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Blood vessel, neoplasm (hemangioma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TT Digestive tract, disease (hemorrhage; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Liver, disease (hepatic adenomatosis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Adenoma (hepatic; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT (hepatocellular; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT (hepatoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Edema (hereditary angioneurotic; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Allergy (hypersensitivity; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Intestine (ileum, cancer; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Myositis (inclusion body; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Heart, disease (infarction; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Protozoa Rickettsia (infection; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Cytomegalovirus (infectivity; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Cardiovascular system, disease (inflammation-related; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Intestine, disease (inflammatory; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TT Eye, disease Spinal cord, disease (injury; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Autoimmune disease (insulin-dependent diabetes mellitus; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TΤ Diabetes mellitus (insulin-dependent; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Pancreatic islet of Langerhans, neoplasm IT (insulinoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Neoplasm (intaepithelial neoplasia; COX-2 inhibitor-TACE inhibitor combination

for treatment of neoplasia, pain, inflammation, and vaso-occlusive

events) тт Neoplasm (interepithelial squamous cell neoplasia; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) ΙT Intestine, disease (irritable bowel syndrome; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) ΙT Brain, disease Heart, disease (ischemia; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) тт Intestine (jejunum, cancer; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Rheumatoid arthritis (juvenile; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TТ Carcinoma (large cell; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TT Myoma (leiomyoma, fibroid tumor; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Mvoma Sarcoma (leiomyosarcoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TТ Spinal cord (lumbar, lumbago; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Eye, disease TТ (macula, degeneration; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Reproductive tract (male, cancer; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TT Brain, neoplasm (medulloblastoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) ΙT Carcinoma (medulloepithelioma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Nervous system, disease (meningeal, cancer; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Menstruation (menstrual cramp; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT , Carcinoma Mesothelium, neoplasm (mesothelioma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Neoplasm (metastasis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TТ Headache (migraine; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Carcinoma (mucoepidermoid; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Muscle, disease

(muscular pain; COX-2 inhibitor-TACE inhibitor combination for

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treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Astrocyte
        (neoplasm, astrocytoma; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Oligodendrocyte
        (neoplasm, oligodendroglioma; COX-2 inhibitor-TACE inhibitor
        combination for treatment of neoplasia, pain, inflammation, and
        vaso-occlusive events)
    Bone marrow, disease
IT
     Gamete and Germ cell
     Spinal cord, disease
        (neoplasm; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
TΤ
     Inflammation
    Kidney, disease
        (nephritis; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
     Kidney, disease
IT
        (nephrotic syndrome; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Nerve, disease
    Pain
        (neuralgia; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Nerve, neoplasm
        (neuroblastoma; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Lymphoma
        (non-Hodgkin's; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Blood vessel, disease
        (occlusion; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IΤ
    Eye, disease
        (ocular angiogenesis; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
    Eye, disease
IT
        (ocular photophobia; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
TТ
    Injury
        (ocular; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
TТ
    Neuroglia, neoplasm
        (oligodendroqlioma; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
ΙT
    Bone, neoplasm
     Sarcoma
        (osteosarcoma; COX-2 inhibitor-TACE inhibitor combination for treatment
        of neoplasia, pain, inflammation, and vaso-occlusive events)
    Tooth, disease
IT
        (pain; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Rheumatic diseases
        (palindromic; COX-2 inhibitor-TACE inhibitor combination for treatment
        of neoplasia, pain, inflammation, and vaso-occlusive events)
TТ
    Ulcer
        (peptic; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Artery, disease
    Inflammation
        (periarteritis nodosa; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Nerve, disease
        (peripheral neuropathy; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Inflammation
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Lung, disease (pneumonitis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TΤ Myositis (polymyositis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TT Disease, animal (polyp; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Surgery (postoperative inflammation and pain; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Parturition (premature; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Prostate gland (prostatic intraepithelial neoplasia; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Sarcoma (pseudosarcoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Arthritis (psoriatic arthritis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) ITLung, neoplasm (pulmonary blastoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) ΙT Carcinoma (pulmonary small-cell; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Lung, disease (pulmonary stenosis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) ΙT (pulmonary; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) ΙT Arthritis (reactive; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) ΙT (rectum, anorectum cancer; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) ΙT Digestive tract, disease (recurrent gastrointestinal lesion; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Kidney, neoplasm Kidney, neoplasm (renal cell carcinoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Carcinoma Carcinoma (renal cell; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) ΙT (resorption, inhibitors; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT (resorption; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events)

Search done by Noble Jarrell

(restenosis; COX-2 inhibitor-TACE inhibitor combination for treatment

of neoplasia, pain, inflammation, and vaso-occlusive events)

IT

Artery, disease

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IT
     Eye, disease
     Inflammation
        (retinitis; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IT
        (retinoblastoma; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Eye, disease
        (retinopathy; COX-2 inhibitor-TACE inhibitor combination for treatment
        of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Blood vessel
        (revascularization procedure inflammation; COX-2 inhibitor-TACE
        inhibitor combination for treatment of neoplasia, pain, inflammation,
        and vaso-occlusive events)
ΙT
    Sarcoma
        (rhabdomyosarcoma; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
ΙT
        (sclera, scleritis; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Connective tissue, disease
        (scleroderma; COX-2 inhibitor-TACE inhibitor combination for treatment
        of neoplasia, pain, inflammation, and vaso-occlusive events)
TТ
    Mental disorder
        (senile psychosis; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
     Shock (circulatory collapse)
IT
        (septic; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Carcinoma
        (serous; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Body, anatomical
        (sinus, cancer; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
TT
    Lung, neoplasm
        (small-cell carcinoma; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Intestine, neoplasm
        (small; COX-2 inhibitor-TACE inhibitor combination for treatment of
        neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Muscle, disease
        (smooth, cancer; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Animal tissue, disease
        (soft, neoplasm; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
TΤ
    Neoplasm
        (soft-tissue; COX-2 inhibitor-TACE inhibitor combination for treatment
        of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Injury
     Nervous system, neoplasm
        (spinal cord; COX-2 inhibitor-TACE inhibitor combination for treatment
        of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     Spinal column, disease
        (spondyloarthropathy; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
тт
    Joint, anatomical
    Muscle
        (sprains and strains; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
ΙT
        (squamous cell; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Medical goods
        (stents, stent placement inflammation; COX-2 inhibitor-TACE inhibitor
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combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TT Ischemia (stroke ischemia; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Brain, disease TT (stroke, stroke ischemia; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Brain, disease (stroke; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Neoplasm (submesothelial; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT (swelling after; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TT Arthritis Synovial membrane, disease (synovitis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) ΤТ Lupus erythematosus (systemic; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Inflammation (tendinitis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Inflammation IT Thyroid gland, disease (thyroiditis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) Transplant and Transplantation (toxicity; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Brain, disease Head, disease (trauma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) TT Digestive tract, disease (ulcer, peptic; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT Inflammation Intestine, disease (ulcerative colitis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) ITCarcinoma (uterine endometrial adenocarcinoma; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) ΤТ Eye, disease Inflammation (uveitis; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) IT (vascular rejection; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and vaso-occlusive events) ΙT Blood vessel, disease Inflammation (vasculitis, systemic rheumatoid; COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia, pain, inflammation, and

vaso-occlusive events)

Blood vessel, disease

Inflammation

IT

(vasculitis; COX-2 inhibitor-TACE inhibitor combination for treatment

of neoplasia, pain, inflammation, and vaso-occlusive events)

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IT
        (venous; COX-2 inhibitor-TACE inhibitor combination for treatment of
       neoplasia, pain, inflammation, and vaso-occlusive events)
IT
        (verrucous; COX-2 inhibitor-TACE inhibitor combination for treatment of
       neoplasia, pain, inflammation, and vaso-occlusive events)
IT
        (viral-induced inflammation; COX-2 inhibitor-TACE inhibitor combination
        for treatment of neoplasia, pain, inflammation, and vaso-occlusive
        events)
    Reproductive organ
IT
        (vulva, cancer; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
TΤ
    Disease, animal
        (white matter disease; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
    Mouth, disease
        (xerostomia; COX-2 inhibitor-TACE inhibitor combination for treatment
        of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
                       329900-75-6, Cyclooxygenase 2
     151769-16-3, TACE
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia,
        pain, inflammation, and vaso-occlusive events)
IT
     71125-38-7, Meloxicam
                            130370-59-1
                                         130370-60-4
                                                        145337-55-9, RO
                            147783-68-4
                                                        162011-90-7, Rofecoxib
    31-9790 147783-67-3
                                          154039-60-8
     163847-77-6 163958-73-4 168158-16-5 169590-41-4, Deracoxib
     169590-42-5, Celecoxib 169799-04-6 181695-72-7, Valdecoxib
     184947-94-2, FYK 1388 187034-31-7
                                         191406-90-3
                                                        191408-36-3
     191613-76-0
                 192329-42-3, Prinomastat
                                            198470-84-7, Parecoxib
     202409-33-4, Etoricoxib 204125-89-3
                                            206547-73-1 209397-76-2
    212609-63-7
                 212609-68-2 215593-63-8
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                 277304-07-1
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     260270-56-2
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           431948-78-6, WTACE2 478911-60-3
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                                                             709648-08-8, TNF
     484
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia,
       pain, inflammation, and vaso-occlusive events)
IT
     64-17-5, Ethanol, biological studies
     RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
        (alc. dementia; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
IT
     9002-04-4, Thrombin
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (hypoprothrombinemia; COX-2 inhibitor-TACE inhibitor combination for
        treatment of neoplasia, pain, inflammation, and vaso-occlusive events)
     51110-01-1, Somatostatin
IT
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (somatostatin-secreting tumor; COX-2 inhibitor-TACE inhibitor
        combination for treatment of neoplasia, pain, inflammation, and
        vaso-occlusive events)
IT
     169799-04-6
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (COX-2 inhibitor-TACE inhibitor combination for treatment of neoplasia,
        pain, inflammation, and vaso-occlusive events)
RN
     169799-04-6 HCAPLUS
CN
     Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-
    pyridinylmethyl)amino]-3-methyl-, monohydrochloride, (2R)- (9CI)
     INDEX NAME)
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Absolute stereochemistry.

HCl

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L30 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2003:757689 HCAPLUS
     139:276755
DN
ED
     Entered STN: 26 Sep 2003
     Preparation of epothilone derivatives for therapeutic use as anticancer
ΤI
     agents
IN
     Regueiro-Ren, Alicia; Kim, Soong-Hoon
     Bristol-Myers Squibb Company, USA
PΑ
     PCT Int. Appl., 47 pp.
SO
     CODEN: PIXXD2
DТ
     Patent
LА
     English
IC
     ICM C07D277-28
     ICS A61K031-425
     26-6 (Biomolecules and Their Synthetic Analogs)
     Section cross-reference(s): 1, 63
FAN.CNT 1
     PATENT NO.
                          KIND
                                 DATE
                                              APPLICATION NO.
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                                 20030925
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
         UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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PRAI US 2002-363441P
                           P
                                  20020312
     WO 2003-US7584
                           W
                                  20030311
CLASS
 PATENT NO.
                  CLASS PATENT FAMILY CLASSIFICATION CODES
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 WO 2003078411
                  ICM
                         C07D277-28
                  ICS
                         A61K031-425
 WO 2003078411
                         A61K031/425; A61K031/425+M; A61K045/06;
                  ECLA
                         C07D417/06+277B+225; C07D493/04+313B+303B
                         417/365.000; 548/204.000
 US 2003191089 NCL
OS MARPAT 139:276755
```

AB Epothilone derivs., such as I [M = bond, O, NR9, CR10R11; X = O, NH; R1-R4 = H, alkyl; R5 = H, alkyl, cyano; R6 = H, alkyl, aryl, heterocyclyl; R9-R11 = H, OH, alkyl, alkoxy, aryl, cycloalkyl, heterocyclyl], pharmaceutically acceptable salts, solvates or hydrate thereof, were prepared for use as antitumor agents. Thus, epothilone derivative II was prepared from 2,3-dehydro epothilone A, via silylation of hydroxyl group, potassium cyanide addition, followed by deprotection. The prepared epothilone derivs. were assayed in vitro for their effect on tubulin polymerization and for cytotoxicity against HCT-116 human colon carcinoma cells. Therapeutic compns. containing I or in combination with other therapeutic agents useful in the treatment of cancer or other proliferative diseases are also claimed.

ST epothilone deriv prepn antitumor

IT Tubulins

RL: BSU (Biological study, unclassified); BIOL (Biological study) (calf brain; preparation of epothilone derivs. for therapeutic use as anticancer agents)

IT Nervous system, neoplasm

(central, treatment; preparation of epothilone derivs. for therapeutic use as anticancer agents)

IT Uterus, neoplasm

(cervix, treatment; preparation of epothilone derivs. for therapeutic use as anticancer agents)

IT Intestine, neoplasm

(colon, treatment; preparation of epothilone derivs. for therapeutic use as anticancer agents)

IT Intestine, neoplasm

(colorectal, treatment; preparation of epothilone derivs. for therapeutic use as anticancer agents)

IT Neoplasm

(metastatic, treatment of; preparation of epothilone derivs. for therapeutic use as anticancer agents)

IT Neoplasm

(neck, treatment; preparation of epothilone derivs. for therapeutic use as anticancer agents)

IT Neck, anatomical

(neoplasm, treatment; preparation of epothilone derivs. for therapeutic use as anticancer agents)

IT Antitumor agents

Asymmetric synthesis and induction

(of epothilone derivs. for therapeutic use as anticancer agents)

IT Interferons

Interleukin 12

Interleukins

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical composition containing epothilone derivs and; preparation of epothilone derivs. for therapeutic use as anticancer agents)

IT Human

IT

(preparation of epothilone derivs. for therapeutic use as anticancer agents)

(solid, treatment; preparation of epothilone derivs. for therapeutic use as

```
anticancer agents)
IT
     Angiogenesis inhibitors
     Bladder, neoplasm
     Bone, neoplasm
     Brain, neoplasm
     Esophagus, neoplasm
     Kidney, neoplasm
Larynx, neoplasm
     Liver, neoplasm
     Lung, neoplasm
     Mammary gland, neoplasm
     Mouth, neoplasm
     Ovary, neoplasm
     Pancreas, neoplasm
     Pharynx, neoplasm
     Pituitary gland, neoplasm
     Prostate gland, neoplasm
       Skin, neoplasm
     Stomach, neoplasm
     Uterus, neoplasm
        (treatment; preparation of epothilone derivs. for therapeutic use as
        anticancer agents)
ΙT
     Interferons
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (\alpha, pharmaceutical composition containing epothilone derive and; preparation of
        epothilone derivs. for therapeutic use as anticancer agents)
IT
     50-07-7, Mitomycin C 50-18-0, Cyclophosphamide 50-44-2, Mercaptopurine
     50-76-0, Actinomycin D 50-91-9, Floxuridine 51-21-8, 5-Fluorouracil
     52-24-4, Thiotepa 52-53-9, Verapamil 54-62-6, Aminopterin 55-86-7, Mechlorethamine hydrochloride 55-98-1, Busulfan 57-22-7, Vincristine
     58-05-9, Leucovorin 59-05-2, Methotrexate 70-51-9, Deferoxamine
     76-60-8, BCG 91-18-9, Pteridine 147-94-4, Cytarabine 148-82-3,
                                                                  299-75-2,
     Melphalan 154-42-7, Thioguanine 154-93-8, Carmustine
     Treosulfan 302-79-4, Tretinoin 305-03-3, Chlorambucil
                                                                   378-44-9
     Betamethasone 518-28-5, Podophyllotoxin 518-28-5D, Podophyllotoxin,
     derivs. 574-93-6, Phthalocyanine 645-05-6, Altretamine 801-52-5,
     Porfiromycin 865-21-4, Vinblastine 1404-04-2, Neomycin
                                                                      2410-93-7,
     Methopterin 2998-57-4, Estramustine 3094-09-5, Doxifluridine
     3562-63-8, Megestrol 3778-73-2, Ifosfamide 4291-63-8, Cladribine
     4342-03-4, Dacarbazine 9041-93-4, Bleomycin sulfate 10540-29-1, Tamoxifen 13010-47-4, Lomustine 13311-84-7, Flutamide 13909-09-6,
                14276-59-6, SI-27, biological studies 14769-73-4, Levamisole
     Semustine
     15228-71-4, Leurosidine 15663-27-1, Cisplatin 15866-90-7, Metastat
     16268-62-5, Pentamethylmelamine
                                        18883-66-4, Streptozocin
                                                                      20830-81-3,
     Daunorubicin 21679-14-1, Fludarabine 22089-22-1, Trofosfamide
     23360-92-1, Leurosine 24280-93-1, Mycophenolic acid 25316-40-9
    Adriamycin 29767-20-2, Teniposide 33069-62-4, Paclitaxel 33419-42-0, Etoposide 36791-04-5, Ribavirin 38101-59-6, IM 862 41575-94-4,
     Carboplatin 48134-75-4, 1-Methyl-4-phenylpyridinium ion 50935-04-1
     51481-61-9, Cimetidine 52128-35-5, Trimetrexate 52205-73-9,
     Estramustine phosphate sodium 53643-48-4, Vindesine 53714-56-0,
     Leuprolide 54083-22-6, Zorubicin 56420-45-2, Epirubicin 57982-77-1, Buserelin 58957-92-9, Idarubicin 62996-74-1, Staurosporine
     65271-80-9, Mitoxantrone 67526-95-8, Thapsigargin 72496-41-4,
     Pirarubicin 75330-75-5, Lovastatin 75425-66-0, Saframycins
     77029-83-5D, Hypocrellin A, demethoxy 84449-90-1, Raloxifene 90357-06-5, Bicalutamide 91421-43-1, 9-Aminocamptothecin 96
                                                                     96389-68-3,
     Crisnatol 97682-44-5, Irinotecan 100286-90-6, Irinotecan hydrochloride
     110942-02-4, Aldesleukin 114899-77-3, Ecteinascidin 743 117091-64-2,
     Etoposide phosphate 118908-07-9, EICAR 122111-03-9, Gemcitabine
     hydrochloride 123948-87-8, Topotecan 125317-39-7, Vinorelbine tartrate
     127943-53-7, Discodermolide 148717-90-2, Squalamine
                                                                153436-54-5, SU
     5271 169799-04-6, CGS-27023A
                                    174722-31-7,
                                             187888-07-9, Endostatin
     Rituximab 180288-69-1, Trastuzumab
     188968-51-6, EMD-121974 192329-42-3, AG-3340 193809-84-6, MMI 166
     204005-46-9, Su 5416 205923-56-4, IMC-C225 252916-29-3, SU 6668
```

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259188-38-0, BMS-275291
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (pharmaceutical composition containing epothilone derivs and; preparation of
        epothilone derivs. for therapeutic use as anticancer agents)
                                                               604799-59-9P
TT
     476623-89-9P
                   476623-90-2P
                                  476623-91-3P
                                                476623-92-4P
     604799-60-2P
                    604799-61-3P
                                   604799-62-4P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
        (preparation of epothilone derivs. for therapeutic use as anticancer agents)
IT
     151-50-8, Potassium cyanide 994-30-9, Triethylsilyl chloride
     226956-20-3
                 226956-21-4 476623-83-3
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of epothilone derivs. for therapeutic use as anticancer agents)
                                 476623-85-5P 476623-86-6P
IT
     247232-02-6P
                   476623-84-4P
                                                                476623-87-7P
     476623-88-8P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of epothilone derivs. for therapeutic use as anticancer agents)
RE.CNT
             THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Ashley; US 6489314 B1 2002 HCAPLUS
(2) Nicolaou; US 6531497 B1 2003 HCAPLUS
     169799-04-6, CGS-27023A
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (pharmaceutical composition containing epothilone derivs and; preparation of
        epothilone derivs. for therapeutic use as anticancer agents)
RN
     169799-04-6 HCAPLUS
     Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-
CN
     pyridinylmethyl)amino]-3-methyl-, monohydrochloride, (2R)- (9CI)
     INDEX NAME)
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Absolute stereochemistry.

HCl

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L30 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     2003:757513 HCAPLUS
DN
     139:276754
ΕD
     Entered STN: 26 Sep 2003
TI
     Preparation of C12-cyano epothilone derivatives with antitumor activity
IN
     Vite, Gregory D.; Regueiro-Ren, Alicia
PA
     Bristol-Myers Squibb Company, USA
SO
     PCT Int. Appl., 47 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
IC
     ICM A61K031-365
     ICS A61K031-425; C07D313-00; C07D315-00; C07D417-06; C07D417-14
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CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 63

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	PATENT NO.										APPLICATION NO.									
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									IN,											
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				TZ,	UA,	UG,	US,	UΖ,	VC,	VN,	YU,	ZA,	ZM,	ZW						
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						A61K031-425; C07D313-00; C07D315-00; C07D417-06;														
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						514/217.030; 514/365.000; 548/181.000; 514/232.800;														
	US	2003	31869	65	NCL															
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					ECL				06+2					/04.	2120	. 202	ь			
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	GI	IAIA1	CPAL .	139:	2/0/) 1														
	GI																			

$$R^{5}$$
 R^{6}
 R^{6}
 R^{1}
 R^{2}
 R^{3}
 R^{2}
 R^{3}
 R^{2}
 R^{3}
 R^{4}
 R^{4

AB Epothilone derivs. of formula I [R1-R5 = H, alkyl; R6 = H, alkyl, aryl, cycloalkyl, heterocyclo; X = H; Y = OH; XY = bond] are prepared Also included are therapeutic compns. containing the compds. of formula I as active ingredients, alone or in combination with other therapeutic agents useful in the treatment of cancer or other proliferative diseases. Thus, II was prepared in several steps from epothilone A. The EC0.01 of the prepared compds. was 0.01 to 1000 μM in in vitro tubulin polymerization assay.

II

```
ST
     epothilone cyano prepn antitumor
    Nervous system, neoplasm
IT
        (central; preparation of C12-cyano epothilone derivs. with antitumor
        activity)
IT
    Uterus, neoplasm
        (cervix; preparation of C12-cyano epothilone derivs. with antitumor
        activity)
     Intestine, neoplasm
TT
        (colon; preparation of C12-cyano epothilone derivs. with antitumor activity)
IT
     Intestine, neoplasm
        (colorectal; preparation of C12-cyano epothilone derivs. with antitumor
        activity)
IT
    Drug delivery systems
        (freeze-dried; preparation of C12-cyano epothilone derivs. with antitumor
        activity)
IT
    Neoplasm
        (neck; preparation of C12-cyano epothilone derivs. with antitumor activity)
IT
    Neck, anatomical
        (neoplasm; preparation of C12-cyano epothilone derivs. with antitumor
        activity)
ΙT
    Lung, neoplasm
        (non-small-cell carcinoma; preparation of C12-cyano epothilone derivs. with
        antitumor activity)
IT
    Angiogenesis
    Angiogenesis inhibitors
    Antitumor agents
    Bladder, neoplasm
    Bone, neoplasm
     Brain, neoplasm
     Esophagus, neoplasm
    Head, neoplasm
    Human
    Kidney, neoplasm
    Larynx, neoplasm
    Liver, neoplasm
    Mammary gland, neoplasm
    Mouth, neoplasm
    Neoplasm
    Ovary, neoplasm
     Pancreas, neoplasm
     Pharynx, neoplasm
     Pituitary gland, neoplasm
     Prostate gland, neoplasm
      Skin, neoplasm
     Stomach, neoplasm
     Uterus, neoplasm
        (preparation of C12-cyano epothilone derivs. with antitumor activity)
IT
    Disease, animal
        (proliferative; preparation of C12-cyano epothilone derivs. with antitumor
        activity)
IT
    Carcinoma
        (pulmonary non-small-cell; preparation of C12-cyano epothilone derivs. with
        antitumor activity)
IT
    Carcinoma
        (pulmonary small-cell; preparation of C12-cyano epothilone derivs. with
        antitumor activity)
ΙT
    Lung, neoplasm
        (small-cell carcinoma; preparation of C12-cyano epothilone derivs. with
        antitumor activity)
ΙT
   Neoplasm
        (solid; preparation of C12-cyano epothilone derivs. with antitumor activity)
IT
    Calcium channel blockers
        (therapeutic agent for use with C12-cyano epothilone derivs.)
IT
     Interferons
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (therapeutic agent for use with C12-cyano epothilone derivs.)
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ΙT
     Interferons
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (α; therapeutic agent for use with C12-cyano epothilone derivs.)
IT
     604772-12-5P
     RL: BYP (Byproduct); PREP (Preparation)
         (preparation of C12-cyano epothilone derivs. with antitumor activity)
IT
                     604772-08-9P
                                      604772-09-0P 604772-10-3P
     604772-07-8P
     RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); RACT (Reactant or reagent); USES (Uses)
         (preparation of C12-cyano epothilone derivs. with antitumor activity)
TT
     476623-94-6P 604772-11-4P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
         (preparation of C12-cyano epothilone derivs. with antitumor activity)
     152044-53-6, Epothilone A
TT
     RL: RCT (Reactant); RACT (Reactant or reagent)
         (preparation of C12-cyano epothilone derivs. with antitumor activity)
     247232-06-0P 247232-07-1P 247232-08-2P 476623-93-5P
TT
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
         (preparation of C12-cyano epothilone derivs. with antitumor activity)
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     50-76-0, Actinomycin D 50-91-9, Floxuridine 51-21-8, 5-Fluorouracil
     52-24-4, Thiotepa 52-53-9, Verapamil 54-62-6, Aminopterin 55-86-7,
     Mechlorethamine hydrochloride 55-98-1, Busulfan 57-22-7, Vincristine
     58-05-9, Leucovorin 59-05-2, Methotrexate 70-51-9, Deferoxamine 76-60-8, BCG 91-18-9, Pteridine 147-94-4, Cytarabine 148-82-3
     Melphalan 154-42-7, Thioguanine 154-93-8, Carmustine Treosulfan 302-79-4, Tretinoin 305-03-3, Chlorambucil
                                                                      299-75-2,
                                                                      378-44-9.
     Betamethasone 518-28-5, Podophyllotoxin 574-93-6, Phthalocyanine
     645-05-6, Altretamine 801-52-5, Porfiromycin 865-21-4, Vinblastine
     1404-04-2, Neomycin 2410-93-7, Methopterin 2998-57-4, Estramustine
     3094-09-5, Doxifluridine 3562-63-8, Megestrol 3778-73-2, Ifosfamide 4291-63-8, Cladribine 4342-03-4, Dacarbazine 9041-93-4, Bleomycin
     sulfate 10540-29-1, Tamoxifen 13010-47-4, Lomustine 13311-84-7, Flutamide 13909-09-6, Semustine 14276-59-6, SI-27, biological studies
     14769-73-4, Levamisole 15228-71-4, Leurosidine 15663-27-1, Cisplatin
     15866-90-7, Metastat 16268-62-5, Pentamethylmelamine 18883-66-4,
     Streptozocin 20830-81-3, Daunorubicin 21679-14-1, Fludarabine
     22089-22-1, Trofosfamide 23360-92-1, Leurosine 24280-93-1,
     Mycophenolic acid 25316-40-9, Adriamycin 29767-20-2, Teniposide
     33069-62-4, Paclitaxel
                               33419-42-0, Etoposide 36791-04-5, Ribavirin
     38101-59-6, IM 862 39472-31-6, Carminomycin 41575-94-4, Carboplatin
     48134-75-4, 1-Methyl-4-phenylpyridinium 51481-61-9, Cimetidine 52128-35-5, Trimetrexate 52205-73-9, Estramustine phosphate sodium 53643-48-4, Vindesine 53714-56-0, Leuprolide 54083-22-6, Zorubicin
     56420-45-2, Epirubicin 57982-77-1, Buserelin
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     60084-10-8, Tiazofurin 62996-74-1, Staurosporine 65271-80-9,
     Mitoxantrone 67526-95-8, Thapsigargin 72496-41-4, Pirarubicin
     75330-75-5, Lovastatin 77029-83-5D, Hypocrellin A, demethoxy derivative 79392-34-0, Saframycin 84449-90-1, Raloxifene 84573-33-1, Quinocarcin
     87578-98-1, Safracin A 87578-99-2, Safracin B
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     91421-43-1, 9-Aminocamptothecin
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               174722-31-7, Rituximab 180288-69-1, Trastuzumab
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     205923-56-4, Cetuximab
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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (therapeutic agent for use with C12-cyano epothilone derivs.) THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT RE (1) Hoefle; US 6262094 B1 2001 HCAPLUS (2) Schering Ag; DE 10020517 A1 2001 HCAPLUS ΙT 169799-04-6, CGS-27023A RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (therapeutic agent for use with C12-cyano epothilone derivs.) RN169799-04-6 HCAPLUS Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-CNpyridinylmethyl)amino]-3-methyl-, monohydrochloride, (2R)- (9CI) INDEX NAME)

Absolute stereochemistry.

HC1

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L30 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
     2003:570772 HCAPLUS
AN
     139:122766
DN
     Entered STN: 25 Jul 2003
ED
     Compositions containing collagen gels and a metalloprotease inhibitor
TI
     Hunter, William L.; Gravett, David M.; Toleikis, Philip M.; Maiti, Arpita
IN
PΑ
     Angiotech Pharmaceuticals, Inc., Can.
SO
     PCT Int. Appl., 62 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
IC
     ICM A61K007-00
CC
      63-6 (Pharmaceuticals)
     Section cross-reference(s): 62
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CLASS
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                        4C206/MA87; 4C206/NA12; 4C206/ZA81; 4C206/ZA89
os
     MARPAT 139:122766
     Compns. comprising collagen and at least one metalloprotease inhibitor,
AB
     and methods of making and using them are provided. The metalloprotease
     inhibitor can be selected from hydroxamic acids such as trocade or
     batimastat. Thus, a composition contained batimastat 1 µg-30 mg/mL of
     injectable collagen/saline suspension.
st
     collagen gel metalloprotease inhibitor
IT
     Medical goods
        (adhesives; compns. containing collagen gels and metalloprotease inhibitor)
TT
     Polymers, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (biodegradable; compns. containing collagen gels and metalloprotease
        inhibitor)
IT
     Polyesters, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (caprolactone-based; compns. containing collagen gels and metalloprotease
        inhibitor)
IT
     Drug delivery systems
     Dyes
     Human
     Lip
     Micelles
        (compns. containing collagen gels and metalloprotease inhibitor)
IT
     Albumins, biological studies
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Carbohydrates, biological studies
       Collagens, biological studies
     Fibrinogens
       Gelatins, biological studies
     Peptides, biological studies
     Polyanhydrides
     Polycarbonates, biological studies
     Polymer blends
     Polysaccharides, biological studies
     Silicone rubber, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (compns. containing collagen gels and metalloprotease inhibitor)
IT
     Polyesters, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (dilactone-based; compns. containing collagen gels and metalloprotease
        inhibitor)
TT
     Drug delivery systems
     Prosthetic materials and Prosthetics
        (implants; compns. containing collagen gels and metalloprotease inhibitor)
TΤ
     Bladder, disease
        (incontinence; compns. containing collagen gels and metalloprotease
        inhibitor)
IT
     Polyesters, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (lactide; compns. containing collagen gels and metalloprotease inhibitor)
IT
     Drug delivery systems
        (liposomes, multilamellar; compns. containing collagen gels and
        metalloprotease inhibitor)
     Drug delivery systems
IT
        (liposomes; compns. containing collagen gels and metalloprotease inhibitor)
IT
     Adhesives
        (medical; compns. containing collagen gels and metalloprotease inhibitor)
IT
     Drug delivery systems
        (microspheres; compns. containing collagen gels and metalloprotease
        inhibitor)
IT
     Polyethers, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (ortho ester group-containing; compns. containing collagen gels and
        metalloprotease inhibitor)
TТ
     Polyoxyalkylenes, biological studies
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (polyester-; compns. containing collagen gels and metalloprotease
        inhibitor)
IT
     Polyesters, biological studies
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (polyoxyalkylene-; compns. containing collagen gels and metalloprotease
        inhibitor)
IT
     Collagens, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (type I; compns. containing collagen gels and metalloprotease inhibitor)
IT
     Collagens, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (type II; compns. containing collagen gels and metalloprotease inhibitor)
TТ
     13598-36-2D, Phosphonic acid, alkylidenebis-derivs.
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (Bisphosphonate; compns. containing collagen gels and metalloprotease
        inhibitor)
IT
     88306-55-2P
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (compns. containing collagen gels and metalloprotease inhibitor)
                             64-75-5, Tetracycline hydrochloride
IT
     60-54-8, Tetracycline
     Acrylic acid, esters, polymers 79-41-4D, Methacrylic acid, esters,
               564-25-0, Doxycycline
                                        9002-04-4, Thrombin
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Cellulose, biological studies 9004-54-0, Dextran, biological studies 9004-61-9, Hyaluronic acid 9004-67-5, Methyl cellulose 9005-25-8, 10118-90-8, Minocycline 10592-13-9, Starch, biological studies Doxycycline hydrochloride 13614-98-7, Minocycline hydrochloride 24937-78-8, EVA 24980-41-4, Polycaprolactone 25248-42-4, Polycaprolactone 26009-03-0, PolyGlycolide 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26202-08-4, PolyGlycolide 26680-10-4, Polylactide 26744-04-7, Poly(3-hydroxybutyric acid), SRU 26780-50-7, Glycolide-lactide copolymer 52352-27-9, Poly(hydroxybutyric 106392-12-5, Polyethylene glycol-polypropylene 86102-31-0, TIMP glycol block copolymer 124861-55-8, TIMP 2 130370-60-4, Batimastat 140208-24-8, TIMP 145809-21-8, TIMP 3 154039-60-8, Marimastat 169799-04-6, CGS-27023A 186207-03-4, TIMP 4 190648-49-8, Trocade 193022-04-7, Ro 1130830 259188-38-0, BMS-275291 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (compns. containing collagen gels and metalloprotease inhibitor) 69494-91-3, Maturase 141907-41-7, Matrix metalloprotease IT RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; compns. containing collagen gels and metalloprotease inhibitor) IT 169799-04-6, CGS-27023A RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (compns. containing collagen gels and metalloprotease inhibitor) RN 169799-04-6 HCAPLUS Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-CN pyridinylmethyl)amino]-3-methyl-, monohydrochloride, (2R)- (9CI) INDEX NAME)

Absolute stereochemistry.

● HCl

L30 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN 2003:300930 HCAPLUS AN DN 138:309229 ED Entered STN: 18 Apr 2003 Improved bone graft TI Knaack, David; Traianedes, Kathy; Diegman, Michele; Forsyth, Nanette; IN Winterbottom, John PΑ Osteotech, Inc., USA SO PCT Int. Appl., 87 pp. CODEN: PIXXD2 DT Patent LΑ English ICM A61L027-00 IC 63-3 (Pharmaceuticals) Section cross-reference(s): 9 FAN.CNT 1 KIND DATE APPLICATION NO. DATE PATENT NO.

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     An improved demineralized bone matrix (DBM) or other matrix composition is
AB
     provided that has been mixed with a stabilizing agent that acts as (1) a
     diffusion barrier, (2) a enzyme inhibitor, (3) a competitive substrate, or
     (4) a masking moiety. A diffusion barrier acts as a barrier so as to
     protect the osteoinductive factors found in DBM from being degraded by
     proteolytic and glycolytic enzymes at the implantation site. Stabilizing
     agents may be any biodegradable material such as starches, modified
     starches, cellulose, dextran, polymers, proteins, and collagen. As the
     stabilizing agents degrades or dissolves in vivo, the osteoinductive
     factors such as TGF-\beta, BMP, and IGF are activated or exposed, and the
     activated factors work to recruit cells from the perivascular space to the
     site of injury and to cause differentiation into bone-forming cells. The
     invention also provides methods of preparing, testing, and using the
     inventive improved osteoinductive matrix compns.
     demineralized bone matrix graft implant TGFbeta IGF BMP
ST
IT
     Bone
         (artificial; improved bone graft comprising a demineralized bone
        matrix)
IT
     Ceramics
         (biocompatible; improved bone graft comprising a demineralized bone
        matrix)
IT
     Transplant and Transplantation
         (bone; improved bone graft comprising a demineralized bone matrix)
IT
     Polymers, biological studies
     RL: DEV (Device component use); TEM (Technical or engineered material
     use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (co-; improved bone graft comprising a demineralized bone matrix)
IT
     Bone
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(demineralized; improved bone graft comprising a demineralized bone
        matrix)
TT
     Polyesters, biological studies
     RL: DEV (Device component use); TEM (Technical or engineered material
     use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (glycolide-based; improved bone graft comprising a demineralized bone
        matrix)
ΙT
     Proteins
     RL: DEV (Device component use); TEM (Technical or engineered material
     use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (growth factor-binding; improved bone graft comprising a demineralized
        bone matrix)
IT
    Alkylating agents, biological
     Antibiotics
    Antitumor agents
     Bone formation
     Diffusion barrier
     Drug delivery systems
     Milling (size reduction)
     Nutrients
     Particle size distribution
     Stabilizing agents
     Virus
    Wound healing promoters
        (improved bone graft comprising a demineralized bone matrix)
TT
    Agglutinins and Lectins
    Alkyl iodides
     Angiogenic factors
    Antibodies and Immunoglobulins
     Biopolymers
     Bone morphogenetic proteins
     Fatty acids, biological studies
     Lipids, biological studies
     Phosphatidylcholines, biological studies
     Polyesters, biological studies
     Polyethers, biological studies
     Polymers, biological studies
     Polysaccharides, biological studies
     Proteins
     Transforming growth factors
     RL: DEV (Device component use); TEM (Technical or engineered material
     use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (improved bone graft comprising a demineralized bone matrix)
     Growth factors, animal
IT
     RL: PEP (Physical, engineering or chemical process); PYP (Physical
     process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);
     USES (Uses).
        (improved bone graft comprising a demineralized bone matrix)
TT
     Growth factors, animal
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (improved bone graft comprising a demineralized bone matrix)
     Enzymes, biological studies
TТ
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (inhibitors; improved bone graft comprising a demineralized bone
        matrix)
IT
     Polyesters, biological studies
     RL: DEV (Device component use); TEM (Technical or engineered material
     use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (lactide; improved bone graft comprising a demineralized bone matrix)
TT
     Sulfhydryl group
        (modifiers; improved bone graft comprising a demineralized bone matrix)
IT
        (muscle of; improved bone graft comprising a demineralized bone matrix)
     Polyethers, biological studies
     RL: DEV (Device component use); TEM (Technical or engineered material
     use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
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(ortho ester group-containing; improved bone graft comprising a
        demineralized bone matrix)
TT
     Growth factors, animal
     RL: DEV (Device component use); TEM (Technical or engineered material
     use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (osteogenins; improved bone graft comprising a demineralized bone
IT
     Oryctolagus cuniculus
        (paravertebral space of; improved bone graft comprising a demineralized
        bone matrix)
ΙT
     Collagens, biological studies
     RL: DEV (Device component use); TEM (Technical or engineered material
     use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (sponge; improved bone graft comprising a demineralized bone matrix)
IT
     Bone
        (transplant; improved bone graft comprising a demineralized bone
        matrix)
IT
     Polycarbonates, biological studies
     RL: DEV (Device component use); TEM (Technical or engineered material
     use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (tyrosine; improved bone graft comprising a demineralized bone matrix)
ΤТ
     Macroglobulins
     RL: DEV (Device component use); TEM (Technical or engineered material
     use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (\alpha 2-, stabilizing agent; improved bone graft comprising a
        demineralized bone matrix)
IT
     9005-82-7, Amylose
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (-resistant starches; improved bone graft comprising a demineralized
        bone matrix)
                                7758-87-4, Tricalcium phosphate
TΤ
     1306-06-5, Hydroxyapatite
     Calcium sulfate 10103-46-5, Calcium phosphate
                                                        13767-12-9, Tetracalcium
     phosphate
     RL: DEV (Device component use); TEM (Technical or engineered material
     use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (ceramics; improved bone graft comprising a demineralized bone matrix)
IT
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     26100-51-6, Polylactic acid
                                  26124-68-5, Polyglycolic acid 34346-01-5,
                                           61912-98-9, Igf
     Lactic acid-glycolic acid copolymer
                                                              81627-83-0, Mcsf
     RL: DEV (Device component use); TEM (Technical or engineered material
     use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (improved bone graft comprising a demineralized bone matrix)
IT
                  130370-60-4 147783-67-3
                                              154039-60-8, BB 2516
     123984-00-9
     162514-46-7, CT1746 169799-04-6, CGS 27023A
                               190648-49-8, Ro 32-3555
                                                           191406-88-9, SE205
     179545-77-8, BAY 12-9566
     192329-42-3, AG3340
                          206547-44-6
                                         259188-38-0
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (improved bone graft comprising a demineralized bone matrix)
     54249-88-6, Dipeptidylpeptidase iv
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (inhibitors, stabilizing agents; improved bone graft comprising a
        demineralized bone matrix)
TT
     9028-35-7
     RL: DEV (Device component use); TEM (Technical or engineered material
     use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (inhibitors, statins; improved bone graft comprising a demineralized
        bone matrix)
                                                     9032-92-2, Glycosidase
TT
     9001-92-7, Proteinase
                             9004-08-4, Cathepsin
     141907-41-7, Matrix metalloproteinase
```

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; improved bone graft comprising a demineralized bone

matrix)

TT 55-91-4, Diisopropylfluorophosphate 60-32-2, ε-Aminocaproic acid 66-71-7, 1,10-Phenanthroline 67-42-5, Egta 128-53-0, N-Ethylmaleimide 329-30-6, 1-Chloro-3-tosylamido-4-phenyl-2-butanone 329-98-6, Phenylmethylsulfonyl fluoride 1670-14-0, Benzamidine hydrochloride 2364-87-6 8001-27-2, Hirudin 9035-81-8, Trypsin inhibitor 9041a1-Antitrypsin 9076-44-2, Chymostatin 9087-70-1, Aprotinin 26305-03-3, Pepstatin a 34284-75-8, 4-(2-Aminoethyl)benzenesulfonyl fluoride 36357-77-4, Phosphoramidon 37691-11-5, Antipain 51798-45-9. Elastatinal 55123-66-5, Leupeptin 58970-76-6, Bestatin 66701-25-5, E-64 76684-89-4, e-64c 76808-15-6, Ebelactone b 76808-16-7, Ebelactone a 88321-09-9, e-64d 90614-48-5, Diprotin a 96551-81-4, Arphamenine A 100157-28-6, Foroxymithine 100938-10-1, Amastatin hydrochloride 103900-19-2, Arphamenine B 110044-82-1, Calpain inhibitor I 110115-07-6, Calpain inhibitor ii 129085-76-3, Leuhistin 134448-10-5, Ca-074 141176-92-3, α1-Antichymotrypsin 187402-73-9, Phebestin 216319-45-8 RL: DEV (Device component use); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (stabilizing agent; improved bone graft comprising a demineralized bone matrix) IT

169799-04-6, CGS 27023A

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (improved bone graft comprising a demineralized bone matrix)

169799-04-6 HCAPLUS RN

CN Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3pyridinylmethyl)amino]-3-methyl-, monohydrochloride, (2R)- (9CI) INDEX NAME)

Absolute stereochemistry.

HCl

L30 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN AN 2001:402131 HCAPLUS DN 135:135176 Entered STN: 05 Jun 2001 EDFunctional role of matrix metalloproteinases (MMPs) in mammary epithelial TΙ cell development Lee, Ping-Ping H.; Hwang, Jiuan-Jiuan; Mead, Lawrence; Ip, Margot M. Grace Center Drug Center, Roswell Park Cancer Institute, Buffalo, NY, AU CS 14263. USA SO Journal of Cellular Physiology (2001), 188(1), 75-88 CODEN: JCLLAX; ISSN: 0021-9541 PB Wiley-Liss, Inc. DTJournal LA English 13-6 (Mammalian Biochemistry) CC Section cross-reference(s): 2

AB The extracellular matrix (ECM) is an important regulator of mammary epithelial cell (MEC) function and is remodeled by matrix metalloproteinases (MMPs). To investigate the significance and regulation of MMP activity in normal MEC, we utilized a primary culture model in which rat MEC were grown three dimensionally within a reconstituted basement membrane (RBM) in defined serum-free medium. Zymograms of culture medium demonstrated that five major gelatinases of 97, 80, 74, 69, and 65 kDa were secreted by MEC and were distinct from gelatinases of RBM origin. Based on mol. weight, p-aminophenylmercuric acid activation, immunoblotting with MMP-specific antibodies, inhibition by EDTA, a peptide containing the prodomain sequence of MMP (TMRKPRCGNPDVAN) and two synthetic MMP inhibitors (BB-94 and CGS 27023A), these were classified as inactive and active forms of MMP-9 and MMP-2. The maximal MMP activities occurred when MEC were in a rapid proliferation and branching phase and declined after they underwent functional differentiation. Known regulators of MEC growth and differentiation were evaluated for their ability to modulate gelatinase activity in primary culture. Secretion of one or both MMPs was inhibited by EGF, $TGF\alpha$, prolactin, and hydrocortisone and stimulated by progesterone. Furthermore, the functional significance of MMPs was demonstrated since three MMP inhibitors blocked branching morphogenesis elicited by the absence of hydrocortisone. Addnl., two synthetic MMP inhibitors not only inhibited epithelial cell growth but also inhibited normal alveolar development of the MEC. Finally, these drugs were found to enhance MMP secretion from MEC, although the activity of the secreted MMPs was inhibited as long as the drug was present. matrix metalloproteinase secretion proliferation differentiation mammary ST epithelium Mammary gland (epithelium; functional role of matrix metalloproteinases (MMPs) in mammary epithelial cell development) IT Cell differentiation Cell proliferation Extracellular matrix (functional role of matrix metalloproteinases (MMPs) in mammary epithelial cell development) Transforming growth factors RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); BIOL (Biological study)

(α-; secretion of matrix metalloproteinases in mammary epithelial cells inhibited by)

146480-36-6, Gelatinase B IT 146480-35-5, Gelatinase A RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(functional role of matrix metalloproteinases (MMPs) in mammary epithelial cell development)

9002-62-4, Prolactin, biological studies 50-23-7, Hydrocortisone 62229-50-9, EGF

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(secretion of matrix metalloproteinases in mammary epithelial cells inhibited by)

IT 57-83-0, Progesterone, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(secretion of matrix metalloproteinases in mammary epithelial cells stimulated by)

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- AN 2000:685535 HCAPLUS
- DN 133:330007
- Entered STN: 29 Sep 2000 ED
- Functional significance of MMP-9 in tumor necrosis factor-induced

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proliferation and branching morphogenesis of mammary epithelial cells
ΔIJ
     Lee, Ping-Ping H.; Hwang, Jiuan-Jiuan; Murphy, Gillian; Ip, Margot M.
     Department of Pharmacology and Therapeutics, Grace Center Drug Center,
     Roswell Park Cancer Institute, Buffalo, NY, 14263, USA
SO
     Endocrinology (2000), 141(10), 3764-3773
     CODEN: ENDOAO; ISSN: 0013-7227
PR
     Endocrine Society
DT
     Journal
LΑ
     English
CC
     2-10 (Mammalian Hormones)
     Section cross-reference(s): 13, 14
     Tissue remodeling is a key process involved in normal mammary gland
AB
     development, with matrix metalloproteinases (MMPs) playing an important
     role in this process. Our laboratory has demonstrated that tumor necrosis
     factor (TNF) stimulates branching morphogenesis of mammary epithelial
     cells (MEC) within a reconstituted basement membrane. Studies
     were therefore undertaken to determine whether MMPs might mediate the effects
     of TNF. Using a primary culture model in which rat MEC grow
     three-dimensionally within a reconstituted basement membrane,
     the authors found that TNF stimulated secretion of MMP-9 but not MMP-2.
     To determine whether MMP-9 was involved in TNF-induced proliferation and
     branching morphogenesis, the authors used a peptide containing the prodomain
     sequence of MMPs and two MMP inhibitors. Both the prodomain peptide
     (5+10-4-10-3 M), as well as BB-94 (10-8-10-5 M) and CGS
     27023A (10-6-10-5 M), inhibited TNF-induced proliferation and
     branching morphogenesis in a concentration-dependent manner. Finally, to verify
     the specific requirement for MMP-9, the authors demonstrated that an MMP-9
     neutralizing antibody blocked TNF-induced proliferation and branching
     morphogenesis. Together, these data suggest that TNF-regulated MMP-9 may
     play a role in the controlled invasion of the fad pad that occurs during
     normal mammary gland development and that misregulation of MMP-9 may
     contribute to the invasiveness of breast cancer.
     MMP9 metalloproteinase tumor necrosis factor proliferation breast
ST
     epithelium; mammary epithelium morphogenesis MMP9 metalloproteinase TNF
IT
     Cell proliferation
        (MMP-9 metalloproteinase mediates tumor necrosis factor-induced
        proliferation and branching morphogenesis of mammary epithelial cells)
IT
     Tumor necrosis factors
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (MMP-9 metalloproteinase mediates tumor necrosis factor-induced
        proliferation and branching morphogenesis of mammary epithelial cells)
IT
     Mammary gland
        (epithelium; MMP-9 metalloproteinase mediates tumor necrosis
        factor-induced proliferation and branching morphogenesis of)
ΙT
     Mammary gland
        (neoplasm; MMP-9 metalloproteinase mediates tumor necrosis
        factor-induced proliferation and branching morphogenesis of mammary
        epithelial cells in relation to)
IT
     146480-36-6, MMP 9
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (MMP-9 metalloproteinase mediates tumor necrosis factor-induced
        proliferation and branching morphogenesis of mammary epithelial cells)
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 - Search done by Noble Jarrell

Stromal fibroblasts interact with invading cancer cells by secreting and

activating matrix metalloproteinases (MMPs). To elucidate the mechanisms

14-1 (Mammalian Pathological Biochemistry)

CC

AB

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involved in the expression and activation patterns of MMPs, human
     colon-cancer cell lines Caco-2 and LoVo and colon-fibroblast cell line
     CCD18-Co were co-cultivated in non-contact and contact conditions which
     mimic in vivo interaction between cancer cells and fibroblasts before and
     after cancer invasion resp. Gelatin zymog. disclosed that MMP-2 was
     secreted from the fibroblasts but not from the cancer cells. The quantity
     of fibroblast-derived MMP-2 in conditioned medium was not significantly
     changed in either the contact or the non-contact co-cultures when compared
     with that of individual cultures of CCD18-Co fibroblasts. Cancer cells in
     non-contact co-cultures, however, enhanced the activation of
     fibroblast-derived MMP-2. Transcripts of membrane-type matrix
     metalloproteinase-1 (MTI-MMP), which is thought to be present on the cell
     surface and to work as a candidate activator of MMP-2, were detected in
     both cancer cell lines. Plasma membrane exts. of cancer cells also
     activated MMP-2 in conditioned media in cell-free conditions. This
     activation of MMP-2 may be caused by MTI-MMP of the cancer cells, since it
     was inhibited by a series of MMP inhibitors, including EDTA, the tissue
     inhibitor of metalloproteinase-2 (TIMP-2), and the MMP inhibitor
     CGS 27023A, but not by TIMP-1. Our data demonstrate
     that in non-contact co-cultures colon-cancer cells activate
     fibroblast-derived MMP-2 on their plasma membranes. These findings should
     help to elucidate the mechanism involved in the initial destruction of
     basement membrane by cancer cells.
     matrix metalloproteinase fibroblast colon cancer plasma membrane
     Intestine, neoplasm
        (colon; non-contact co-culture human colon-cancer cells activate
        fibroblast-derived MMP-2 on their plasma membranes)
     Cell membrane
     Fibroblast
        (non-contact co-culture human colon-cancer cells activate
        fibroblast-derived MMP-2 on their plasma membranes)
     RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
     BIOL (Biological study); OCCU (Occurrence)
        (non-contact co-culture human colon-cancer cells activate
        fibroblast-derived MMP-2 on their plasma membranes)
     124861-55-8, TIMP-2 146480-35-5, Matrix metalloproteinase-2
     161384-17-4, Membrane-type matrix metalloproteinase-1
     RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
     BIOL (Biological study); OCCU (Occurrence)
        (non-contact co-culture human colon-cancer cells activate
        fibroblast-derived MMP-2 on their plasma membranes)
RE.CNT
       33
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study); PREP (Preparation); PROC (Process)

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(catalytic activities and substrate specificity of human membrane type
        4 matrix metalloproteinase (MT4-MMP) catalytic domain)
                                          66-71-7, 1,10-Phenanthroline
     60-00-4, EDTA, biological studies
     106314-87-8, u 24522 130370-60-4, Batimastat 142880-36-2, Galardin
     154039-60-8, Marimastat 169799-04-6, CGS
     27023A
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     148969-98-6, Progelatinase A
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     (Biological study); PROC (Process)
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        4 matrix metalloproteinase (MT4-MMP) catalytic domain)
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     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
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     Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-
CN
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INDEX NAME)

Absolute stereochemistry.

HCl

with $IL-1\alpha$)

Cartilage

IT

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ΑN
DN
     132:58874
     Entered STN: 02 Aug 1999
ED
ΤI
     Matrix metalloproteinase inhibitor CGS 27023A protects
     COMP and proteoglycan in the bovine articular cartilage but not the
     release of their fragments from cartilage after prolonged stimulation in
     vitro with IL-1α
ΑU
     Ganu, Vishwas; Melton, Richard; Wang, Weigwang; Roberts, Don
     Arthritis and Bone Metabolism, Novartis Institute for Biomedical Research,
CS
     Summit, NJ, 07901, USA
SO
     Annals of the New York Academy of Sciences (1999),
     878 (Inhibition of Matrix Metalloproteinases), 607-611
     CODEN: ANYAA9; ISSN: 0077-8923
     New York Academy of Sciences
PB
DT
     Journal
     English
LΑ
     1-7 (Pharmacology)
CC
AB
     In arthritis, the metalloproteinases (MP) such as stromelysin-1,
     collagenase-1 and -3, MT1-MMP, 92-kDa gelatinase, amd as yet unidentified
     MP aggrecanase are thought to play a role in the degradation of proteoglycans
     (PG), cartilage oligomeric matrix protein (COMP), and type II collagen,
     the components of articular cartilage. The MMP inhibitors CGS
     27023A and BB-94 are potent inhibitors of several MPs, but only
     BB-94 inhibits aggrecanase activity. The authors investigated whether
     this two activities is needed in protecting the cartilage components PG
     and COMP.
ST
     antiarthritic CGS27023A BB94 MMP inhibitor proteoglycan; COMP
     CGS27023A BB94 MMP inhibitor arthritis
     Antiarthritics
     Arthritis
        (MMP inhibitor CGS 27023A protects COMP and
        proteoglycan in the bovine articular cartilage but not the release of
        their fragments from cartilage after prolonged stimulation in vitro
        with IL-1\alpha)
IT
     Proteoglycans, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (MMP inhibitor CGS 27023A protects COMP and
        proteoglycan in the bovine articular cartilage but not the release of
        their fragments from cartilage after prolonged stimulation in vitro
```

and proteoglycan in the bovine articular cartilage but not the release

(articular; MMP inhibitor CGS 27023A protects COMP

```
of their fragments from cartilage after prolonged stimulation in vitro
        with IL-1\alpha)
IT
     Proteins, specific or class
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (matrix, cartilage oligomeric; MMP inhibitor CGS
        27023A protects COMP and proteoglycan in the bovine articular
        cartilage but not the release of their fragments from cartilage after
        prolonged stimulation in vitro with IL-1\alpha)
IT
     Collagens, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (type II; MMP inhibitor CGS 27023A protects COMP
        and proteoglycan in the bovine articular cartilage but not the release
        of their fragments from cartilage after prolonged stimulation in vitro
        with IL-1\alpha)
IT
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     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
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        proteoglycan in the bovine articular cartilage but not the release of
        their fragments from cartilage after prolonged stimulation in vitro
        with IL-1\alpha)
     79955-99-0, Stromelysin-1 146480-36-6, 92-KDa gelatinase
                                                                  147172-61-0,
                  161384-17-4, MT1-MMP 175449-82-8, Collagenase-3
     Aggrecanase
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
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        proteoglycan in the bovine articular cartilage but not the release of
        their fragments from cartilage after prolonged stimulation in vitro
        with IL-1\alpha)
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     9001-12-1, Collagenase
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        their fragments from cartilage after prolonged stimulation in vitro
        with IL-1\alpha)
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Absolute stereochemistry.

HCl

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     Angiotensin-converting enzyme inhibitor-matrix metalloproteinase inhibitor
TI
     combinations for treatment of fibrosis, ventricular dilation, and heart
     Peterson, Joseph Thomas, Jr.; Pressler, Milton Lethan
IN
PA
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     1-12 (Pharmacology)
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CLASS

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PATENT NO.
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OS
    MARPAT 131:68144
    Combinations of ACE inhibitors and MMP inhibitors are useful to slow and
AR
     reverse the process of fibrosis, ventricular dilation, and heart failure
     in mammals.
    ACE inhibitor combination fibrosis cardiovascular agent; matrix
ST
    metalloproteinase inhibitor combination fibrosis cardiovascular agent; MMP
    ACE inhibitor fibrosis cardiovascular agent
IT
    Antihypertensives
     Cardiovascular agents
    Drug delivery systems
    Fibrosis
     Keloid
        (ACE inhibitor-matrix metalloproteinase inhibitor combinations for
        treatment of fibrosis, ventricular dilation, and heart failure)
TT
     Peritoneum
     Peritoneum
        (adhesion; ACE inhibitor-matrix metalloproteinase inhibitor
        combinations for treatment of fibrosis, ventricular dilation, and heart
        failure)
     Reproductive tract
IT
        (adnexitis, fibrosis associated with; ACE inhibitor-matrix
        metalloproteinase inhibitor combinations for treatment of fibrosis,
        ventricular dilation, and heart failure)
     Respiratory distress syndrome
IT
        (adult, fibrosis associated with; ACE inhibitor-matrix metalloproteinase
        inhibitor combinations for treatment of fibrosis, ventricular dilation,
        and heart failure)
IT
     Spinal column
        (ankylosing spondylitis, fibrosis associated with; ACE inhibitor-matrix
        metalloproteinase inhibitor combinations for treatment of fibrosis,
        ventricular dilation, and heart failure)
IT
     Intestine, disease
        (bowel stricture; ACE inhibitor-matrix metalloproteinase inhibitor
        combinations for treatment of fibrosis, ventricular dilation, and heart
        failure)
TT
     Heart, disease
        (cardiomyopathy, dilated, fibrosis associated with; ACE inhibitor-matrix
        metalloproteinase inhibitor combinations for treatment of fibrosis,
        ventricular dilation, and heart failure)
TT
     Biliary tract
     Esophagus
        (disease, stricture; ACE inhibitor-matrix metalloproteinase inhibitor
        combinations for treatment of fibrosis, ventricular dilation, and heart
        failure)
IT
     Heart, disease
        (failure; ACE inhibitor-matrix metalloproteinase inhibitor combinations
        for treatment of fibrosis, ventricular dilation, and heart failure)
TТ
     Arteriosclerosis
     Cardiovascular system
     Cirrhosis
     Inflammation
        (fibrosis associated with; ACE inhibitor-matrix metalloproteinase
        inhibitor combinations for treatment of fibrosis, ventricular dilation,
        and heart failure)
     Lung, disease
IT
        (fibrosis; ACE inhibitor-matrix metalloproteinase inhibitor
```

combinations for treatment of fibrosis, ventricular dilation, and heart failure)

IT Kidney, disease

(glomerulosclerosis; ACE inhibitor-matrix metalloproteinase inhibitor combinations for treatment of fibrosis, ventricular dilation, and heart failure)

IT Skin, disease

(hypertrophic scar; ACE inhibitor-matrix metalloproteinase inhibitor combinations for treatment of fibrosis, ventricular dilation, and heart failure)

IT Drug delivery systems

(parenterals; ACE inhibitor-matrix metalloproteinase inhibitor combinations for treatment of fibrosis, ventricular dilation, and heart failure)

IT Adhesion, biological

Adhesion, biological

(peritoneal; ACE inhibitor-matrix metalloproteinase inhibitor combinations for treatment of fibrosis, ventricular dilation, and heart failure)

IT Heart, disease

(rheumatic, fibrosis associated with; ACE inhibitor-matrix metalloproteinase inhibitor combinations for treatment of fibrosis, ventricular dilation, and heart failure)

IT Connective tissue

(scleroderma, fibrosis associated with; ACE inhibitor-matrix metalloproteinase inhibitor combinations for treatment of fibrosis, ventricular dilation, and heart failure)

IT Drug delivery systems

(solns., oral; ACE inhibitor-matrix metalloproteinase inhibitor combinations for treatment of fibrosis, ventricular dilation, and heart failure)

IT Ureter

Urethra

(stricture; ACE inhibitor-matrix metalloproteinase inhibitor combinations for treatment of fibrosis, ventricular dilation, and heart failure)

IT Drug interactions

(synergistic; ACE inhibitor-matrix metalloproteinase inhibitor combinations for treatment of fibrosis, ventricular dilation, and heart failure)

IT Drug delivery systems

(tablets; ACE inhibitor-matrix metalloproteinase inhibitor combinations for treatment of fibrosis, ventricular dilation, and heart failure)

IT Heart, disease

(valve, fibrosis associated with; ACE inhibitor-matrix metalloproteinase inhibitor combinations for treatment of fibrosis, ventricular dilation, and heart failure)

IT Heart

(ventricle, ventricular dilation; ACE inhibitor-matrix metalloproteinase inhibitor combinations for treatment of fibrosis, ventricular dilation, and heart failure)

ΙT 47081-89-0 62571-86-2, Captopril 74258-86-9, Alacepril 75847-73-3. 76420-72-9, Enalaprilat 76547-98-3, Lisinopril 80830-42-8. Enalapril 81872-10-8, Zofenopril 82586-55-8, Quinapril hydrochloride Rentiapril 82834-16-0, Perindopril 82924-03-6, Pentopril 82768-85-2, Quinaprilat 83647-97-6, Spirapril 85441-61-8, Quinapril 83435-66-9, Delapril 87679-37-6, Trandolapril 88768-40-5, Cilazapril 87333-19-5, Ramipril 98045-17-1 98045-20-6 98048-97-6, Fosinopril 98045-15-9 103775-10-6, Moexipril 106314-87-8, U24522 111223-26-8, Ceranapril 130370-60-4, Batimastat 142880-36-2, Galardin 111902-57-9, Temocapril 145337-55-9, RO-31-9790 169799-04-6, CGS 191474-90-5 191474-86-9 191474-96-1 191474-84-7 27023A 192807-19-5 192807-26-4 199850-67-4, PD 191475-02-2 192807-13-9 203384-23-0 199850-70-9 199850-76-5 166793-0000 199850-69-6 203384-31-0 203384-26-3 203384-27-4 203384-30-9 204251-87-6 204251-88-7 204251-89-8 204440-64-2 204440-65-3 204769-62-0

208042-05-1 209164-46-5, CDP-845 209200-45-3 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ACE inhibitor-matrix metalloproteinase inhibitor combinations for treatment of fibrosis, ventricular dilation, and heart failure)
9001-12-1, Matrix metalloproteinase 1 79955-99-0, Matrix metalloproteinase 3 141256-52-2, Matrix metalloproteinase 7
141907-41-7, Matrix metalloproteinase 146480-35-5, Matrix

metalloproteinase 2 146480-36-6, Matrix metalloproteinase 9 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(ACE inhibitor-matrix metalloproteinase inhibitor combinations for treatment of fibrosis, ventricular dilation, and heart failure)

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; ACE inhibitor-matrix metalloproteinase inhibitor
combinations for treatment of fibrosis, ventricular dilation, and heart
failure)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD RE

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- (5) Searle & Co; WO 9624373 A 1996 HCAPLUS
- (6) Warner Lambert Co; WO 9744315 A 1997 HCAPLUS
- IT 169799-04-6, CGS 27023A

TT

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ACE inhibitor-matrix metalloproteinase inhibitor combinations for treatment of fibrosis, ventricular dilation, and heart failure)

RN 169799-04-6 HCAPLUS

CN Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-pyridinylmethyl)amino]-3-methyl-, monohydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

L30 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN AN 1997:124446 HCAPLUS

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DN
     126:135633
     Entered STN: 24 Feb 1997
ED
     Arylsulfonamido-substituted hydroxamic acids for the treatment of tumors
TI
     Macpherson, Lawrence Joseph; Parker, David Thomas
IN
     Ciba-Geigy A.-G., Switz.
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     PCT Int. Appl., 53 pp.
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         W: AL, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR,
             TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
             IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
             MR, NE, SN, TD, TG
                                            US 1995-475166
                                                                    19950607 <--
     US 5646167
                                19970708
                         Α
                                          AU 1996-61249
                                                                   19960604 <--
     AU 9661249
                                19961230
                          A1
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PRAI US 1995-475166
                                19950607 <--
     US 1993-1136
                         A2 19930106 <--
     US 1994-265296
US 1994-333676
                        A2
                                19940624 <--
                          A2
                                19941103 <--
19960604 <--
     WO 1996-EP2418
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CLASS
 PATENT NO.
                 CLASS PATENT FAMILY CLASSIFICATION CODES
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                        A61K031-18
 WO 9640101
                 TCM
                        A61K031-33; A61K031-495; A61K031-535; A61K031-54;
                 TCS
                        A61K031-445; A61K031-40; A61K031-335; A61K031-38;
                        A61K031-55; A61K031-47; A61K031-42; A61K031-425
                        A61K031/18; A61K031/4409; A61K031/443; A61K031/445+A;
 WO 9640101
                 ECLA
                        A61K031/341; A61K031/381; A61K031/44+A; A61K031/4402;
                        A61K031/4406
                        514/357.000; 546/336.000; 546/337.000
                 NCL
 US 5646167
                        A61K031/18; C07C311/42; C07D207/09; C07D207/16;
                 ECLA
                        C07D211/26; C07D211/34; C07D211/58; C07D211/66;
                        C07D213/42C; C07D215/12; C07D223/10; C07D233/24;
                        C07D257/04D2C4; C07D261/10B; C07D277/06; C07D277/28;
                        C07D307/16; C07D309/14; C07D313/18; C07D317/58; C07D317/62; C07D333/58; C07D335/02; C07D401/04+213+211;
                        C07D401/12+213+211; C07D401/12+223+213;
                        C07D401/12+233+213; C07D405/12+307+213;
                        C07D405/12+309+213; C07D405/12+307B+213;
                        C07D405/12+313+213; C07D413/12+277B+233;
                        C07D413/12+317+233; C07D521/00B1N2; A61K031/341;
                        A61K031/381; A61K031/44+A; A61K031/4402; A61K031/4406;
                        A61K031/4409; A61K031/443; A61K031/445+A; C07C311/19;
                        C07C311/29
os
     MARPAT 126:135633
     The invention relates to the use of compds. NH(OH)COCR1R2N(CH2R)SO2X (X =
AΒ
     carbocyclic or heterocyclic aryl; R, R1 = H, substituted lower alkyl,
     arylalkyl, biaryl, etc; R2 = H, lower alkyl) for the treatment of a tumor
     selected from human breast carcinoma, lung carcinoma, bladder carcinoma,
     colon carcinoma, prostate carcinoma, skin carcinoma, and ovarian
     carcinoma. N-hydroxy-2(R)-[[4-methoxybenzenesulfonyl](3-picolyl)-amino]-3-
     methylbutanamide·HCl was prepared and formulated into a capsule.
     arylsulfonylaminohydroxyalkanamide prepn antitumor agent
ST
     Antitumor agents
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(bladder carcinoma; arylsulfonamido-substituted hydroxamic acids for
        treatment of tumors)
TT
    Drug delivery systems
        (capsules; arylsulfonamido-substituted hydroxamic acids for treatment
        of tumors)
IT
    Bladder
    Lung, neoplasm
    Mammary gland
    Ovary, neoplasm
     Prostate gland
       Skin, neoplasm
       Skin, neoplasm
        (carcinoma, inhibitors; arylsulfonamido-substituted hydroxamic acids
        for treatment of tumors)
IT
    Antitumor agents
        (colon carcinoma; arylsulfonamido-substituted hydroxamic acids for
        treatment of tumors)
IT
     Intestine, neoplasm
        (colon, carcinoma, inhibitors; arylsulfonamido-substituted hydroxamic
        acids for treatment of tumors)
IT
    Antitumor agents
        (lung carcinoma; arylsulfonamido-substituted hydroxamic acids for
        treatment of tumors)
IT
    Antitumor agents
        (mammary gland carcinoma; arylsulfonamido-substituted hydroxamic acids
        for treatment of tumors)
IT
    Antitumor agents
        (ovary carcinoma; arylsulfonamido-substituted hydroxamic acids for
        treatment of tumors)
IT
    Antitumor agents
        (prostate carcinoma; arylsulfonamido-substituted hydroxamic acids for
        treatment of tumors)
ΙT
    Antitumor agents
    Antitumor agents
        (skin carcinoma; arylsulfonamido-substituted hydroxamic acids for
        treatment of tumors)
IT
     69739-34-0 177702-28-2
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (arylsulfonamido-substituted hydroxamic acids for treatment of tumors)
                                  177702-31-7P
     177702-29-3P
                   177702-30-6P
                                                  177702-32-8P
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (arylsulfonamido-substituted hydroxamic acids for treatment of tumors)
IT
                                                                 177702-35-1P
    177702-09-9P
                   177702-18-0P
                                   177702-33-9P
                                                  177702-34-0P
    177702-37-3P
                   186416-88-6P
                                   186416-89-7P
                                                  186416-90-0P
    RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (arylsulfonamido-substituted hydroxamic acids for treatment of tumors)
IT
    161314-70-1
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    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (arylsulfonamido-substituted hydroxamic acids for treatment of tumors)
IT
    161314-70-1
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (arylsulfonamido-substituted hydroxamic acids for treatment of tumors)
RN
    161314-70-1 HCAPLUS
CN
    Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3-
    pyridinylmethyl)amino]-3-methyl-, (2R)- (9CI) (CA INDEX NAME)
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Absolute stereochemistry.

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L30 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
    1995:819729 HCAPLUS
AN
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DN 123:306168

ED Entered STN: 28 Sep 1995

Metalloprotease inhibitors halt collagen breakdown in IL-1 induced bovine TI nasal cartilage cultures

Spirito, S.; Doughty, J.; O'Byrne, E.; Ganu, V.; Goldberg, R. L. ΑU

CS Research Department, Ciba-Geigy Corp., Summit, NJ, 07901, USA

Inflammation Research (1995), 44 (Suppl. 2), S131-S132 SO CODEN: INREFB; ISSN: 1023-3830

PΒ Birkhaeuser

Journal DT

LΑ English

CC 1-7 (Pharmacology)

AB The 2 matrix metalloprotease inhibitors CGS 27023A and Ro 31-9790 inhibited the loss of collagen from IL-1-treated cartilage organ cultures. They were not effective in blocking the IL-1-induced loss of proteoglycan.

stmetalloprotease inhibitor cartilage collagen breakdown prevention; CGS27023A Ro319790 cartilage collagen proteoglycan

TT Cartilage

> (metalloprotease inhibitors halt collagen breakdown in IL-1-treated cartilage cultures)

Collagens, biological studies TT

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(metalloprotease inhibitors halt collagen breakdown in IL-1-treated cartilage cultures)

TT Lymphokines and Cytokines

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(interleukin 1, metalloprotease inhibitors halt collagen breakdown in IL-1-treated cartilage cultures)

IT 145337-55-9, Ro 31-9790 169799-04-6, CGS 27023A

> RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(metalloprotease inhibitors halt collagen breakdown in IL-1-treated cartilage cultures)

IT 81669-70-7, Metalloprotease

RL: BSU (Biological study, unclassified); BIOL (Biological study) (metalloprotease inhibitors halt collagen breakdown in IL-1-treated cartilage cultures)

IT 169799-04-6, CGS 27023A

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(metalloprotease inhibitors halt collagen breakdown in IL-1-treated cartilage cultures)

RN

169799-04-6 HCAPLUS
Butanamide, N-hydroxy-2-[[(4-methoxyphenyl)sulfonyl](3pyridinylmethyl)amino]-3-methyl-, monohydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

HCl

=> b home FILE 'HOME' ENTERED AT 12:01:00 ON 11 AUG 2005

CN